



# ANNALS of SURGERY

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## INTERNATIONAL CONTRIBUTIONS

TO THE

## STUDY OF CANCER

IN HONOR OF

JAMES EWING

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*Edited by*

LEWIS STEPHEN PILCHER, M.D., LL.D.

AND

FRANK E. ADAIR, M.D.

ARRANGED IN FOUR PARTS

PART I. CANCER IN ITS GENERAL RELATIONS

PART II. CANCER RESEARCH

PART III. REGIONAL CANCER

PART IV. RADIUM AND RÖNTGEN RAY THERAPY

WITH CONTRIBUTIONS FROM  
THE FOLLOWING COUNTRIES

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#### ANNALS OF SURGERY

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## AN APPRECIATION

THIS volume, in honor of James Ewing, serves the twofold purpose of a tribute to one of the leading active pathologists of the world who is likewise the foremost American investigator of the entire group of neoplastic diseases, and of a contribution of great value to the subject of cancer. Did the conditions of a homage volume permit the dedicatee to present a paper the value of the contribution would be still further enhanced.

In a note on the development of the homage volume published in the *Bulletin of the American Association of University Professors*\* Professor Morley formulates a code of ethics for a *Festschrift* as follows:

1. The dedicatee should be recognized as an international leader in his field of research.
2. He should be an eminent trainer of scholars, as well as himself an eminent scholar.
3. These conditions being fulfilled, the recipient would naturally have attained, as the French say, a certain age—about sixty-five, the retiring age in many colleges, which is a natural milestone, though it has not often been observed.
4. The contributors should be former pupils and colleagues and workers in the same specific field; friends they should be, but not admitted only because they are friends.
5. The volume should be as carefully edited as any professional journal, and no article admitted which does not reach that standard.

Every one of these conditions is fully met in this volume. Carefully edited by Doctor Adair, it is a tribute by colleagues and workers in the special field of cancer to Professor James Ewing, an eminent scholar, an eminent trainer of scholars, an international leader in pathology, especially in the field of the cancerous diseases upon the attainment of his sixty-fourth birthday, December 25, 1930.

After his graduation as Bachelor of Arts from Amherst College in 1888, and as Doctor of Medicine from Columbia University in 1891, Doctor Ewing enjoyed for seven or eight years the admirable opportunities for training and experience in pathology furnished by Doctor Prudden's laboratory at the College of Physicians and Surgeons, Columbia University, where he served successively as Tutor, Fellow and Instructor before assuming the duties of the Professorship of Pathology at the Medical School of Cornell University in New York, to which he was called in 1899—a chair which he has occupied with remarkable success both as teacher and investigator for thirty-one years.

Not the least of the memorable services to medical education and the advancement of pathology and public health in this country of that great pioneer of modern pathology in America, T. Mitchell Prudden, was the inspiration,

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\* Vol. xv, No. 4, p. 293, April, 1929.



training and direction which he imparted to an able and devoted group of pupils and assistants during his incumbency of the Chair of Pathology at Columbia University for three decades from 1879 to 1909. The most eminent disciple of this school to carry on and extend the work of the master is the one to whom this volume is dedicated.

While this volume especially signalizes the value of Doctor Ewing's studies in the large and important field of malignant new growths there is scarcely a domain in pathology which he has not cultivated, be it morphological, chemical, clinical or experimental. In this brief introduction to a volume devoted exclusively to cancer no attempt can be made to enumerate the contributions made by Doctor Ewing to pathology in over one hundred and fifty papers, monographs and textbooks. In his early studies, especially those upon the blood, he revealed that interest and competence in cytology which have remained a distinguished mark of his researches for the last quarter of a century upon tumors, and are strikingly exemplified in his important textbook "Neoplastic Diseases," first issued in 1919 and now in its third edition.

Doctor Ewing early recognized the vast and growing significance of the problem of cancer, or as he has properly and effectively taught us to say, "the *problems* of the cancerous or neoplastic diseases"; and he likewise early discerned the importance of attacking these problems by combined pathological and clinical studies, indeed from every promising angle of approach. The width of range represented by the writers and papers in this volume dedicated to a pathologist typify the far-flung interests and the breadth of view of Doctor Ewing himself in all aspects of the subject of malignant diseases.

Not the least of Doctor Ewing's services is that while his pronouncements in the diagnosis of cancer are authoritative, he has exerted a wholesome critical and restraining influence upon hasty generalizations and undue optimism in the interpretation of pathological, etiological and clinical investigations and work. That such measured and considered statements are especially important at the present time is evident when one bears in mind that cancer is today the outstanding problem in medicine and public health; that it threatens the ascendancy of all other causes of death; that its study engages the attention of workers in all fields of medicine and surgery and does not escape the attention, even of biologists remote from medicine; that increase of opportunities for such study makes an especially strong appeal for more generous financial support; and that education both of the medical profession and of the public is the most essential part of the present active campaign for the prevention and cure of cancer.

In the failure to unlock the ultimate secret of the causation of cancer one is likely to overlook the fact that there are few diseases concerning which more additions to our knowledge have been made in the last half century than in the group of cancerous diseases. The so-called "cancer campaign" is abundantly justified by the strikingly improved results of treatment by radical surgery or by radiotherapy attendant upon early diagnosis and prompt

## AN APPRECIATION

treatment. Nor is there any reason to be hopeless regarding a deeper insight into the causation of these diseases.

As a fellow pathologist, in behalf of the contributors to this volume as well as of all students, of the problems here considered, and of a host of pupils, colleagues, friends and admirers, I venture to congratulate Doctor Ewing upon the sixty-fourth anniversary of his birth, to felicitate him upon his many years of fruitful and beneficent activities as teacher, investigator and writer, and to wish him many years of happiness and of continued influence and service in the advancement of useful knowledge.

WILLIAM H. WELCH,  
Johns Hopkins University, Baltimore, Md.



## FOREWORD

THE purpose of this volume is to honor a man who has devoted the largest part of his life and professional career to the investigation of that mystery-disease, cancer. No tribute to such a man could be more appropriate than a *Festschrift* on the subject which lies nearest his heart. During the past decade, cancer has made most alarming progress in civilized countries; and in America since 1928 it is exceeded in death-rate only by heart disease and pneumonia. The problems of cancer are so numerous, so widely divergent and so baffling that it seems timely to assemble the most recent knowledge on the various subjects of cancer research, pathology, surgery and radiotherapy from the scattered clinics and laboratories of Europe and America.

When this suggestion was made to many of the international authorities, they, although burdened by the responsibilities and demands of their work, responded with hearty enthusiasm. Accompanying their scientific contributions were many notes which expressed the authors' admiration, respect and affection for Doctor Ewing. As an example we shall quote the letter of Professor W. Lazarus-Barlow:

*My dear Ewing:*

A Festival number is something unusual and so I have no scruples about prefacing the contribution I am proud to make to it, with a few personal words.

I should like to assure you of the great affection and respect with which you are regarded by myself and, I am convinced, all pathologists in Great Britain. You will not, I am sure, take it wrongly, when I say that we feel there is something in your method of approaching subjects and in your mental attitude which appeals in the strongest degree to our Old World conservatism and caution. Truth is so elusive and has so many facets that repeated verification of observations, care in drawing deductions and, above all, caution in publication seem to be essential if we are not to be snowed under by an avalanche of ill-digested material. These qualities you possess in a very high degree and on that account, amongst others, you are exercising a profoundly beneficial effect upon medical literature. I hope that you will long live to exercise that influence and that you will accept my contribution as a small token of my great regard.

Yours very sincerely  
W. S. LAZARUS-BARLOW

West Mersea, Essex, England  
May 1st, 1930

As a man Ewing is simple in habits and tastes; sincere; intensely loyal; helpful to colleagues; possessing a subtle humor; a lover of competitive sports; tactful in the handling of men and opposing forces; scientifically resourceful and imaginative; optimistic always; idealistic in his belief in men; indulgent to a fault; having an unusual sense of fairness; scientifically aggressive and persistent; one who welcomes and encourages new avenues of approach to problems; a tireless worker; a severe but constructive critic;

discriminating in his estimate of scientific contributions; a stimulating teacher; a forceful lecturer; an indefatigable contributor to scientific movements; a scholar beloved by students and colleagues; a physician of the highest ideals.

The study which he made of radiated tissue is the basis of his strong support of radiotherapy. Radiology and radiotherapy in America owe a great debt to Ewing.

The original members of the Bone Sarcoma Registry of the American College of Surgeons freely admit that Ewing's enthusiastic support kept this monumental work from perishing by neglect. His broad clinical experience and diagnostic acumen have made him a unique figure among American pathologists.

Probably his greatest scientific contribution is his book "Neoplastic Diseases." It is the standard reference and textbook of the world on that subject. The magnitude of assembling all the known facts about neoplastic diseases and subjecting them to a critical and orderly analysis would have daunted any man of ordinary courage. The need was great, the opportunity available, and so for ten years Ewing worked with zealous ardor, holidays, nights, week-ends, stopping for minutes only to fight the paroxysms of tic douloureux. And so did Ewing persevere and work. Today his "Neoplastic Diseases" is a monument to his systematic intellect and his genius.

The relationship of Ewing to the Memorial Hospital can best be expressed in the words of Emerson—"Every institution is but the lengthened shadow of some man." Doctor Ewing *is* the Memorial Hospital.

We wish to express our great appreciation to Dr. Lewis S. Pilcher, Editor of the ANNALS OF SURGERY, who so warmly welcomed our suggestion of this volume; and who has been so indulgent and helpful in the editorial work.

Our gratitude goes out to the J. B. Lippincott Company who found us utterly despondent before certain difficulties of our undertaking, and whose suggestion made this opus possible.

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December, 1930.

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# I

## CANCER IN ITS GENERAL RELATIONS

- SIR G. LENTHIAL CHEATLE, K.C.B., C.V.O., F.R.C.S. London, England  
Lecturer in Surgery, Kings College Hospital and Surgeon to Kings College Hospital.
- "Natural Law in Pathological Growth."
- CLARENCE C. LITTLE, Sc.D. Bar Harbor, Maine  
Director of the American Society for the Control of Cancer.
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- WILLIAM J. MAYO, M.D. Rochester, Minn.  
Chief of the Mayo Clinic.
- "Susceptibility to Cancer."
- W. CRAMER, M.D. London, England  
Director of the Imperial Cancer Research Fund.
- "Resistance and Susceptibility to Cancer."
- H. T. DEELMAN, M.D. Groningen, Holland  
Professor of Pathology, University of Groningen.
- "Heredity and Cancer. A Statistical Study."
- WILLY MEYER, M.D. New York, N. Y.  
Consulting Surgeon to the Lenox Hill and Post Graduate Hospitals.
- "Is Cancer a Systemic Disease?"
- MAUD SLYE Chicago, Ill.  
Director of the Cancer Laboratory of the Otho. S. A. Sprague Memorial Institute and the University of Chicago.
- "The Interrelation between Hereditary Predisposition and External Factors in the Causation of Cancer."
- FREDERICK L. HOFFMAN, LL.D. Wellesley Hills, Mass.  
Consulting Statistician, Prudential Insurance Company of America.
- "Cancer and Smoking Habits."
- WILLIAM SAMPSON-HANDLEY, M.S., F.R.C.S. London, England  
Surgeon to the Middlesex Hospital.
- "The Evidence of Lymphangitis in Papillomata."
- F. BLUMENTHAL, M.D. Berlin, Germany  
Director of the Cancer Institute of University of Berlin.
- "Erzeugung von bösartigen Tumoren durch Einspritzen von Milzbrei und Blut von tumortragenden Rabben und Maussen."
- WILLIAM B. COLEY, M.D. New York, N. Y.  
Attending Surgeon, Memorial Hospital.  
Surgeon-in-chief, Hospital for the Ruptured and Crippled.
- "Multiple Myeloma."
- GUSTAV ROUSSY, M.D. Paris, France  
Professeur à la Faculté and Directeur de Centre Anticancereux de Villejoif.
- "La Metaplasie épithéliale et ses rapports avec les tumeurs."
- GEORGE W. CRILE, M.D. Cleveland, Ohio  
Emeritus Professor of Surgery, Western Reserve Medical School; Chief of the Cleveland Clinic.
- "Treatment of Malignancy."
- EVERETT L. BISHOP, M.D. Atlanta, Ga.  
"Epidermoid Carcinoma in Sebaceous Cysts."
- ROBERT B. GREENOUGH, M.D. Boston, Mass.  
Director of Harvard Cancer Commission; Chief Surgeon to the Huntington Cancer Hospital.
- "Cancer Service in Massachusetts."
- EDWARD B. ELLIS New York, N. Y.  
Chief Technician, Memorial Hospital Laboratories.
- "The Relation of the Technician to the Pathologist."

# INTERNATIONAL CONTRIBUTIONS

TO THE

## STUDY OF CANCER

IN HONOR OF

JAMES EWING

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### NATURAL LAW IN PATHOLOGICAL GROWTH

BY SIR G. LENTHAL CHEATLE, F.R.C.S.

OF LONDON, ENG.

INTRODUCTION.—The definite control over the formation of pathological epithelial new growths is a remarkable feature of their existence. This control is universal and more marked in the benign epithelial new formations than in the malignant types. In carcinoma it is not so universal nor so marked except in certain examples. Let me draw particular attention to the benign epithelial new formations. In all benign epithelial new growths the nature of control they exhibit is identical with the normal conditions of physiological new formations. The control, however, is imperfect. The tissues and seats of new formations may be localized to parts where the process of new formation of a similar character is occurring normally elsewhere in the same glands. For example, the same epithelial and connective tissues that are actively forming in a breast at the age of puberty may at one part or more than one part be forming a type of fibroadenoma. In this tumor new ducts and acini may develop in far greater proportion than in the parts that are normal. These new ducts and acini may be normal in size, shape and appearance while others are irregular in these respects. At other times new and nearly normal formations may occur when the rest of the glands are at rest.

However great are the variations in the normal activities of tissues in which the new formations occur or the varieties of their seats of origin in them, there is exhibited a control of development and structure that is akin to the physiological process. The new formations resemble in structure the physiological growth that occurs in the respective glands and tissues in which they grow.

Another fact should be borne in mind in considering natural law and pathological growth. And it concerns the normal functions that govern the uses of a cell apart from the laws that govern the structure of which it is a part.



The normal uses and functions of all varieties of cells have a marked influence upon morphological appearances of tissues when they become pathological. Take, for example, a fibrous connective tissue cell and three varieties of epithelial cells. Desquamation takes no normal part in the function of a fibrous connective tissue cell and it exhibits desquamation in none of its pathological lesions.

The normal functions of an epidermic cell belonging to the horny layer involve its being constantly shed and renewed. In pathological lesions of the skin the desquamating effects of these epithelial cells alone are seen in dermoid cysts when the walls of which contain no hair follicles nor sebaceous glands.

The normal function of an epithelial cell of the breast entails its being shed for the purposes of elaborating the secretion of milk. The normal shedding of epithelial cells for the purpose of elaborating secretion is also taking place in the prostate and sebaceous glands. In the pathology of breast, sebaceous and prostate glands cystic states depend upon the shedding of desquamating epithelium. Cysts thus formed are consequently very common in these glands.

The function of an epithelial cell in the intestine, kidney, adrenal glands and liver does not include its being shed for the purposes of elaborating either their secretions or excretions as may be. Cysts due to epithelial hyperplasia and neoplasia are uncommon in these viscera principally because epithelial desquamation plays no part of their normal function.

For thirty years I have studied the breast and other glands by cutting them into whole microscopical sections. The study particularly included normal breasts from birth onwards and all forms of diseases that affect the mammary gland. The accessibility and frequency of disease of the breast always made it appeal to me as being an ideal structure to study. The study of a diseased or normal gland always appeared to me to be inefficient unless the whole of it were presented to the observer in microscopical sections of the entire gland. Many important points have been discovered by means of this process. By not having limited myself to the study of breasts alone I can see opportunities for fresh discoveries in other glands and tissues of the body if they are examined by the same method. This method of study proves that although the organs and tissues of the body differ from each other in function and structure there are the same pathological processes affecting them all. The chief differences between them are ordained by their differences in function and structure; for example, a gland containing ducts and acini differs from that which contains only acini or alveoli by the additional changes that occur in the ducts.

The breast and thyroid glands undergo precisely similar changes of adenomatous tumors, cystic formations and malignant diseases. The chief differences between the pathological changes occurring in them are caused by the presence of ducts in the breast. Mr. R. S. Wale and I have recently pointed out that the pathological changes in breasts and prostate glands are

very similar: both, for example, pass through all the changes of a disease Schimmelbusch first called attention to as existing in the breast.\*

The pathological changes in the gastro-intestinal mucous membrane differ from those of the breast, thyroid and prostate glands only by the differences in structure and function. The epithelial elements in all of them undergo similar desquamative epithelial hyperplasia and benign and malignant epithelial neoplasia. The similarity between the pathological changes in breasts and intestinal epithelium are striking. For example, an adenoma of the intestine resembles an adenoma that has formed in a duct of the breast. Because a duct of the breast is so small in calibre that a growing tumor within it induces its dilatation it has given rise to the erroneous, misleading nomenclature of "intracystic adenoma." Adenoma of the colon occurs in a tube of so large a calibre that it cannot be dilated sufficiently to lead the observer into the false position of believing it to be an "intracystic" tumor.

It is interesting to realize how common it is for most epithelium to form papillomata and to see how the differences in function and structure of the epithelium composing them lead to changes which differ from each other in the different glands and tissues only in those respects. For example, first let me take the papillomata that arise in the epithelium of the ducts in the breast. The function of the epithelium of the breast is to secrete and increase the area of glandular secreting surfaces on different occasions during life. As a rule the papillomata of the breast begin by an ingrowth of two or more stalks of pericanalicular connective tissue taking in with them the elastica of the duct wall. The stalks are covered by two layers of epithelium, giving rise to a multiradicular papilloma. These stalks branch and their branches may grow without showing an early tendency to anastomose with each other or with those of neighboring stalks. On the other hand two stunted papillomata may lean toward each other immediately upon their formation and anastomose before any branch has appeared, giving rise to a small cavity or acinus lined by epithelium which at once loses its columnar shape and becomes cuboidal. The cavities that are formed by the anastomoses of neighboring branches of a more developed papilloma are larger and more irregular, but still exhibit the same changes of columnar cells into those which are cuboidal in shape. These changes may be so complete that I have examples of papillomata that contain complete arrangements of ducts lined by columnar epithelium and acini lined by cuboidal epithelium. These are the altered papillomata that have given rise to the misleading term of "intracystic adenomata." In some of these tumors carcinoma has begun. The differences in morphological appearance between them and the papillomata and adenomata of the colon depend only upon their difference in structure and function.

The papillomata growing from the pelvis of the kidney, the urinary bladder, the epidermis and those arising from the ducts of the breast and the colon are chiefly due to the differences in structure and of function. The

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functions of the epithelium of the pelvis of the kidney, urinary bladder and epidermis are chiefly those of providing a covering or lining surface. The functions of breast epithelium are a great deal more complicated and at puberty and lactation it has to form new glandular elements.

It is remarkable that a wart of the skin consists only of epidermic cells and contains no glandular elements or hair follicles of the skin that exist in such profusion over its whole distribution. A wart of the skin is a pathological process that selects and affects the epidermic cells only. The function of the epithelial cells of the epidermis is to cover surfaces.

While new glandular formation is in progress in normal breasts at puberty a fibroadenoma may occur that consists of precisely the same tissues that are undergoing physiological activity elsewhere in the gland. There can be no doubt that the same influences controlling the normal physiological state are in a disturbed degree also controlling the formation of the tumor. The same type of fibroadenoma occurs in mazoplasia when the same tissues of the gland are active when they should be at rest. The same tissues that are active at puberty are also active in mazoplasia in the breasts of non-pregnant women at thirty-five or forty. The activity of mazoplasia may be distributed equally over the whole breast, but it is not so regular as it is at puberty. New ducts and acini and pericanalicular and periacinous connective tissue hyperplasia occur in both conditions.

Pure adenomata also are examples of new breast formation in tumors in which there is only a slight new connective tissue constituent.

The remarkable intracanalicular fibroadenoma, the connective tissue element of which is provided by the subepithelial connective tissue that exists between the epithelial cells and the elastica, is a striking example of a tumor in which beautiful new breast elements are formed. I have described these tumors as occurring in the breasts of women who are generally older than those in whom occur the pericanalicular and periacinous connective tissue fibroadenomata of puberty. As the subepithelial tissue of these tumors bulges into the duct in sessile shapes it is covered by the duct epithelium. From the surface of the tumor secondary papillomata may arise. But what is to me the most interesting thing about these tumors is that the surface epithelium often dips down into the underlying connective tissue and forms clusters of beautifully formed, lusty acini of which any young breast might well be proud. They are joined to the surface by a cellular tube of epithelial cells to form a duct. One of these tumors containing these beautiful glandular formations occurred in an intracanalicular tumor of a woman aged fifty-two years. All sorts of speculations arise from this fact into which I do not intend to enter. Without speculation it can be said with obvious truth that the new glandular formations in the normal development of a breast and in breasts of puberty and pregnancy are subject to normal physiological control. The new glandular formations I have just described in the different kinds of fibroadenomata, however normal they may be in arrangement and appearance, cannot be considered as being normal. Yet they are under some power-

ful, deliberate control which is not far removed from a purely physiological and functional one. All these tumors appear to be benign at their periods of conception. The fibroadenomata and adenomata remain benign throughout their histories in the vast majority of examples, and should they become malignant it is their connective tissue elements which become anaplastic and either morphologically appear to be sarcomatous or actually develop metastatic growths.

Papillomata, on the other hand, are not so consistent in their maintenance of the benign state and their careers are definitely and commonly associated with the termination in carcinoma. The benign tumors upon which I have been speaking are only less under control than the normal processes to which I have compared them, but they are under a control closely resembling the normal one in many essential features.

It is a question whether these benign tumors should be so definitely delimited from each other as they are in the textbooks and in the present outlook with which they are regarded. I believe these tumors are bound together etiologically by their attempts to reproduce normal structures and functions. A striking feature common to these benign tumors is their capacity of being multiple in origin.

It is not so common to discover either sarcoma or carcinoma arising from multicentric sources of origin. The source of these diseases is usually limited to one part of a tissue or gland in the body. When carcinoma occurs in a gland its source is usually limited to one part only.

I have five unusual specimens of breast carcinoma which bear on this point. The whole of the glandular epithelium in all the ducts and acini in all of these specimens is in a state of malignant and highly anaplastic neoplasia. In four of the specimens carcinoma has occurred in one area only. In the remaining one there is regression of the neoplasia and no invasion by epithelial cells into outside tissues.

It is unfortunate that the only test that can be applied to establish the condition of what is called carcinoma is that of epithelial cellular invasion. I am convinced that the biological change of malignancy begins before it manifests itself by infiltrative growth into outside tissues. Directly this manifestation occurs the state is recognizable as being one of carcinoma. The primary tumor from which the infiltrating cells are derived is contained within normal boundaries and can be seen in early specimens of breast carcinoma. The epithelial cellular invasion is only a secondary matter, so far as the process of carcinoma be concerned, although it is of such fatal importance concerning the future of a patient.

The carcinomata that may affect the thyroid, adrenal and thymus glands often cannot be distinguished morphologically or functionally from the normal structure of these glands. Thus even carcinoma can afford the same evidence as the benign tumors I have been alluding to, in that it also may assume methods of growth and function that are present in the normal

physiological states. The fact of there being evidence of physiological control in benign and carcinomatous tumors, however imperfect it may be compared to the perfect control that exists in the development and growth of normal structures, naturally leads to the question of whether it throws any light upon the etiology of either benign or carcinomatous tumors. The failure of being able to adduce decisive experimental evidence compels the answer to be completely speculative and unsatisfactory and further compels all who are interested in the subject to maintain a mind open to all the known and unknown theories that wrack and may wrack respectively all consideration upon the matter. A step toward its solution would be attained if carcinoma always could be traced, passing gradually from a benign state into the malignant one. The process would indicate a progressive transformation in which the appearance of each stage depended upon the stage by which it has been immediately preceded.

There is, in fact, an indication of a progressive process of this kind in the remarkable disease described as Schimmelbusch's disease of the breast in which there is a sequence of events that ends in carcinoma in about 20 per cent. of all cases of carcinoma of the breast. The disease as I translate it begins as a desquamative epithelial hyperplasia which causes cysts. This stage of the disease begins in the late twenty and early thirty years of life and may not pass into the next stage. When it passes on, the next event occurs in the late thirty and early forty years of life and consists of a radical change in the biology of epithelial growth which becomes neoplastic, all the epithelial cells of which are viable and are contained within normal but distended boundaries. The formation of papillomata is a marked feature of this stage. The change from desquamative epithelial hyperplasia into epithelial neoplasia can be seen in all stages of accomplishment. The disease may stop at this stage. When it passes into carcinoma, as it may do, the passage occurs in the late forty and early fifty years of life. In such specimens all three stages of the transition can be traced definitely. On first consideration the process appears to be a definite gradual transition from innocence into malignancy by means of three definite stages which occupy about twenty or thirty years to mature. During the transit the papillomatous growths may exhibit so marked a control and ordination of development that they contain actual duct and acinous structures.

Here again five questions arise: (1) Whether the march of events is only a definite consecutive process? (2) Whether the sequence of events is induced by the continuous action of the same factors? (3) Whether the advent of each event is induced by a completely different factor? (4) Whether all the stages of transformation are due to a disturbed intrinsic physiological process? And (5) whether an extrinsic factor can induce pathological changes that exhibit more than suspicion of physiological control? The last question is the only one that space allows me to discuss.

I will begin by drawing attention to a fibroma that Dr. A. M. Begg dis-

covered in a fowl.\* The tumor looked innocent and was so hard in consistence that he was unable to pound it into a pulp for purposes of filtration. He transplanted this tumor and during its subsequent transplantations it became softer and metastasis occurred. The tumor also became filterable and the filtrate reproduced highly malignant tumors upon inoculation. This tumor may have been either malignant from the beginning of its career or subsequent passages may have made it become so, or some other factor may have entered the arena and created the change in the biological state of the tumor cells.

Fantastic as the notion may first appear, there may be no such thing as a benign tumor, but really all may be malignant and their careers may be interrupted or stopped at any stage.

The signs of physiological control in benign and malignant tumors does not lend any support to the theory that, in consequence, tumors cannot be due to the introduction of an outside agent. The examples of the introduction of outside agents, such as spermatozoon, mechanical irritation and alteration in diet, leading to physiological growth in various examples are too obvious to need recapitulation.

Turning to this question of the genesis of carcinoma, it is one in which I have a completely open, not to say vacant, mind. Yet there are one or two examples of epithelial neoplasia that end in carcinoma into the genesis of which the introduction of an outside agent as a causal factor cannot help creeping into one's mind.

When only one whole duct of a breast and all its branches is picked out as the site for the growth of epithelial neoplasia, its site is so localized that it looks like the accidental incidence or the selection by design of an outside causative factor. This remarkable distribution of epithelial neoplasia occurs in certain examples of papillomata of the breast.

There is another instance which affords the same suggestion of an outside agent being in coöperation with the development of an epithelial neoplasia. The underlying breast of Paget's disease of the nipple develops epithelial neoplasia in many of its parts, sometimes papillomata, sometimes epithelial neoplasia that morphologically appears to be malignant but still confined within normal boundaries, and at other times carcinoma itself.

Paget's disease of the nipple is an affection of the epidermis only of the nipple which extends to the surrounding epidermis of the skin. This fact has been proved by Dr. R. J. Ludford in one recent case of mine. This is what he says:

"I have examined this case of Sir Lenthal Cheate's as completely as possible from a cytological standpoint. The cytological examination proves that Paget's disease of the nipple is a purely epidermic condition, the cells of which could not have been derived from the mammary carcinoma cells of the underlying tumor.

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\* *British Journal of Experimental Pathology*, vol. x, p. 322, 1929.

"During the course of the cytological examination the cells of the carcinoma in the breast and those of Paget's disease of the nipple have been investigated: (1) The chromophility of the cytoplasm (three methods). (2) The cell lipoids, including mitochondria (two methods). (3) The Golgi bodies. (4) The chromatin, as demonstrated by Feulgen's reaction for thymus-nucleic acid.

"All stages of transition of epidermic cells were seen to be taking place in the same microscopic field from normal cells onwards. There are no malignant cells from the breast tumor in the epidermis in the area of Paget's disease."

The chief and most interesting point about Paget's disease of the nipple is always—so far as my experience goes—associated with one of the forms of epithelial neoplasia I have already mentioned. The occurrence and variety of these forms suggest the introduction of an outside agent. Paget's disease of the nipple and the carcinoma of the underlying breast is the strongest example I know that acts as a support for the notion that the introduction of an outside agent can be the cause of biological changes that end in carcinoma.

Finally, the above observations indicate the existence of a systemic control over the formation and genesis of benign and malignant tumors. Is the nature of this control merely one of hereditary tendencies upon the affected cells, or are they influenced by a disturbance in the normal action of internal secretions? There is considerable experimental evidence to show that epithelial and connective tissue hyperplasia may be induced by over-activity of the corpus luteum. This action of the corpus luteum is capable of being prolonged by hormones in the anterior lobe of the pituitary gland. The relation of these hormones to diseases of the breast can be—for the moment—only inferred.

The chief notion pervading this article was drawn particular attention to by Dr. C. W. Nicholson in his classical little book upon "The Nature of Tumor Formation." In his book Doctor Nicholson generously points out that we were thinking about and publishing the same notion at the same time.

# THE PRESENT STATUS OF THE CANCER PROBLEM

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FROM THE ROSCOE B. JACKSON MEMORIAL LABORATORY

ALL SORTS of agencies, individual and institutional, have for years been interested in the investigation of the complex of processes, dealing with research, education, and therapeutics which we may describe as the cancer problem.

Although few, if any, very startling discoveries have been recorded, the sum total of gradual progress has been considerable. It certainly seems to justify us in hoping that within the next few decades there will be still further advances in our knowledge of the nature of the processes which constitute the uncontrolled growth of the tissue of human beings—known as cancer. It is also to be hoped that wherever and whenever possible the efforts of research workers, public health officers, medical men, and the public-minded lay citizen will be highly coöperative. This is extremely desirable because as a result of the complexity of the problem and the great diversity in type of the various agents investigating it, there is a real need for the development of consolidated and unified points of view and for agencies to make the application of such points of view possible.

With this in mind it may be well from time to time to focus our attention on a general analysis of the main features of the problem as a whole with a view to clarifying the situation and to correlating the various efforts which are being made.

Any one of a number of methods of describing, grouping and classifying the different items which together constitute the total problem might be used. Since, however, obstacles to progress are so common in cancer work, it may be well to base our analysis on a consideration of certain of the lines of work which may have grown up as a natural result of the focus of interest on the part of many investigators and clinicians. Lines of work originating without preconceived plan represent, in a way, an indication of the actual terrain—the high and low points, the fertile and sterile areas in the problem. We may fairly inquire as to the general fields of work in one or more of which progress must be made if order is to be brought out of chaos and the organization of the problem be made possible.

There are at least four great fields of the work in which new advances are necessary. More satisfactory and complete methods of classifying and of differentiating between the various types and degrees of cancerous growth will have to be established. The best possible methods of treatment must, of course, constantly be subjected to close scrutiny with a view to improvement and refinement and to the development of new lines of attack. Besides



this there is the immensely important work of attempting to decrease the incidence of cancer by education of the layman in the value of prompt report, early treatment, and the avoidance of causes of needless and obvious irritation. Finally as a fourth problem there is the cause or causes of uncontrolled cancerous growth. The nature of this phase of the subject is such that it obviously demands and will continue to require long periods of painstaking research.

It may seem that it should be easy to make progress in all these lines, but such is not actually the case. Let us see whether we can visualize the factors entering into the situation and acting as obstacles.

In attempting to discover the cause or causes of cancer we have been greatly handicapped by our continued procedure of considering this phase of the problem as one of medical nature. The fact that some of the ordinary theories or tests might prove applicable to cancer has never been entirely lost sight of. Repeated and always unsuccessful efforts to discover a micro-organism which should prove to be the chief causative agent of cancer have been made. In a somewhat similar fashion those who first tried to determine the rôle of heredity in the production of cancer made the great mistake of attempting to prove or to disprove not only the major question of its inheritance, but the number of Mendelian factors involved, by studies of human pedigrees. Evidence of that indirect sort, involving, as it does, much of the quality of rumor, imperfect records, and hearsay, lacks the accuracy which is essential in experimental scientific work. It can be used in a general statistical way to considerable advantage but neither its collection nor its interpretation is a matter primarily medical in nature.

Even when the long-delayed shift from the study of second-hand human data to first-hand experiments with animals in the laboratory was made, the further mistake was made of ignoring essential methods of genetic control. Stock animals obtained from a single dealer, or caught in a single locality are not sufficiently uniform genetically to be used for genetic experiments on cancer. Many large experiments are, however, recorded in scientific publications where even less than the above mentioned is attempted. As a result contradictory and inconclusive findings have delayed our advances and have served to complicate the question of heredity still further than was necessary.

To mention another confusing factor, only recently have we reached a point where we can state first, that biologically there are many forms of cancer; second, that each type thoroughly investigated with adequately controlled material seems to depend in part at least upon constitutional factors which are inherited; third, that the exact type of inheritance is complex and very likely is different in different types of cancer. These statements are not hard to understand if one keeps in mind the fact that many different types of tissue are involved in the various sorts of cancer and that agents which result in abnormal growth of one sort of tissue may quite possibly leave another type entirely unaffected.

Reasoning from analogy and from the human data on record, one may

conclude that studies of heredity may well prove to be one of the most successful means of analyzing the cause or causes of cancer; but that because there are many types of cancer biologically different, as a practical force in preventing its dissemination in man by control and application to individual cases, heredity will not prove to be extremely important.

This does not mean, however, that careful records of every possible individual and family should not be kept and that in special cases heredity may not become a factor worthy of consideration. The efforts now being made in most western countries to gather more complete vital statistics are, therefore, in every way commendable. By more accurate and more extensive vital statistics we are able to detect at as early a date as possible any correlations existing between cancer and age, race, sex, occupation, and a whole grist of abnormal or pathological conditions of anatomy or of physiology. Furthermore, such studies give us the only reliable basis for determining the actual increase or decrease of the incidence of cancer of any given type. Improved methods of diagnosis, a higher percentage of hospitalization, the extension of the average period of life, and more and better autopsies are all factors that may contribute to *recognition* of cancer. This in turn may give the appearance of an actual *increase* in cancer incidence, although it may not have increased in the least.

In the broad field of detection and classification of cancer, human material as it comes to the clinic, hospital or pathologist, can be used advantageously.

Successful efforts to develop a method of yearly diagnosis by which the presence of cancer can be detected at much earlier stages than are at present possible would be a great advance in saving life. Rumors of the discovery of such a test are frequently recurrent. None, however, has as yet been formally accepted by the medical profession.

The classification of cancer by the physiological manifestation of its vigor and virulence, as shown by its rate of growth, frequency of metastasis and invasion of normal tissues, also needs much further study. It is entirely probable that the successful growth of human cancer cells *in vitro* will be followed by advances in all these fields of investigation.

The questions of genetics, of diagnosis and of classification together form a group which may be said to depend very largely on the extent of our knowledge of the nature of the internal environment of the individual in the laboratory or clinic, as the case may be. Recent studies in experimental morphology and embryology are beginning to give us a preliminary picture of the complex relationships which exist inside the body of a mammal. We are still far from being in a position to understand the situation, but a beginning has been made. As a result the importance of the various physiological elements which contribute to the development and control of such processes as growth is becoming more and more clearly recognized.

In matters of treatment we meet for the first time the trained medical worker in direct contact with the cancer problem. The use of surgery,

radium and X-rays—forming as it does the trio of generally recognized treatments—is well known to all.

Any technic of removal of a cancer, whether by the actual cutting of surgery or the burning by X-rays or radium, has the unavoidable danger of being incomplete even when practised by a highly skilful person. To that is added, in the case of radium and X-rays, the danger of injuring the normal tissue or even of stimulating abnormal growth in regions surrounding the destroyed area. This does not mean that surgery, radium or X-rays do not effect cures in certain cases. In fact it has been repeatedly shown that they may. It does mean that the experimental efforts to improve methods of measuring the dosage of X-rays and radium and of applying them should be continued and increased until all sources of error which can be eliminated have been done away with. Further work with electro-surgery will also have to be done. In this connection a very natural and sometimes desirable conservatism of the medical profession which makes it slow to accept any new technical methods may have to be combated.

To aid in the practical solution of this question the organization of clinical centres where the best possible diagnosis and treatment of cancer can be had is needed at or near all large centres of population. As a forerunner of this the studies of hospital and radium facilities now being made by the American Society for the Control of Cancer are significant. So also is the work of the American College of Surgeons which has taken up the task of outlining what it feels to be adequate hospital facilities and of inspecting hospital units to determine whether they meet the requirements.

Undoubtedly the various geographic units, whether they be states, counties, or municipalities, will need individual study and treatment. The work of the American Society for the Control of Cancer has already progressed far enough to show that any general method applied without discrimination would not be successful in every case. Another source of weakness is that there are surprisingly few hospitals in the United States in which anything resembling an adequate "follow-up" method as regards cancer patients is attempted. This condition must be corrected and an attitude of patient research which recognizes the essential nature of long-continued records must be developed. It is hard to make investigators interested in collecting data for later generations to use, but it must be done in the case of such a late-developing condition as cancer.

In all these problems the need of larger numbers of better trained medical men is paramount. Because of many reasons, among which the difficult and discouraging nature of cancer itself is undoubtedly one, the medical schools and active medical profession give much too little attention to training would-be or young doctors in the problem of cancer. Instead of recognizing the challenge offered by cancer as being an outstanding menace about which pathetically little is known and for the combating of which the utmost coöperation is needed, the medical profession fights shy of grappling with the problem and looks for easier foes to conquer. This attitude will have to

be corrected. The spread of popular interest in cancer, coupled with a marked decrease in ignorant fear and superstition concerning it, will undoubtedly in the near future result in a popular demand by the laity for better equipped medical men to cope with the situation. Then, if not before, medical schools and the medical profession as a whole will take the long overdue steps toward more up-to-date and extensive training of their personnel.

In matters involving education of the public, care should always be exercised not to make overenthusiastic claims nor to arouse false hopes. Public educational campaigns always should be preceded by a survey of clinical and hospital facilities, and the form which the educational campaign should take in any locality should depend very largely on what such a survey reveals.

The public is eager for information about cancer. It is gullible and quickly aroused. Caution and patience are necessary in dealing with laymen when cancer is the topic under consideration. For this reason it is especially unfortunate that the ethics of the so-called profession of journalism should be, in many cases, as poorly developed as they are. The newspapers have, in numerous instances, been the means of undoing much of the good which might have accrued from carefully worked-out campaigns of education. By the publication of quack cancer "cures" and the premature, unintelligent and overenthusiastic publicity on many "new treatments" the press has built up unfounded hopes to be followed by a bad mental reaction in thousands and tens of thousands of people. Headlines that use the "selling" phrases of sensationalism; articles that are based on an almost negligible foundation of scientific knowledge are among their sins. The better journals are not so much to blame. They have tried honestly to paint a true picture of the situation and have been and are willing to be cautious and reasonable. Unfortunately there are, however, enough popular second-rate or third-rate sheets to discredit and handicap efforts at public education in the field of cancer work.

Much can and will be done by teaching the public to avoid unnecessary and possibly dangerous irritants and to report suspicious signs of potential cancer at the earliest possible date to some reputable physician or at some accredited hospital.

Taken as a whole it would seem that those interested in the cancer problem have cause for encouragement. The increase in biological knowledge has begun to give us a picture of what controls and shapes the course of growth. The support of state and Federal departments of health which can serve as the means of collecting and studying a superior type of vital statistics is increasing. The greater urbanization which exists all over the country gives a chance for great and able centres of clinical work and hospitalization of cancer cases. The wider spread of education makes the public less difficult to approach in any campaign of information. Finally the interest in public health and the point of view of the preventive medicine "attitude" are reforming and revitalizing our national life in such a way as to make possible a steady increase in the investigation of cancer and in the speed of our progress toward its eventual control.

# SUSCEPTIBILITY TO CANCER

BY WILLIAM J. MAYO, M.D.

OF ROCHESTER, MINNESOTA

THE impressive statistics showing that cancer in the human species is increasing are at least open to question. Reliable computations show that a greater number of persons live to reach middle age or longer, when cancer is more common.

In countries that compile trustworthy statistics the incidence of cancer is approximately in the same ratio to population and sex, but there is considerable divergence in the different organs and tissues involved. In this country, about 30 per cent. of deaths from cancer among women is due to cancer of the breast and genitalia. In men the incidence in the genitalia is very low. On the basis of cancer of the generative organs, therefore, one would expect the total incidence of cancer in men to be considerably lower than in women, but the percentage is approximately the same, because in men the organs common to both sexes, such as the stomach and the organs of the urinary system, are more often affected by cancer than in women, and this increased frequency equalizes the high percentage of instances in which the breasts and uterus are the seat of cancer in women.

One of the few known facts about cancer is its relation to later life. In women the senile changes which take place in the breasts and uterus at the menopause are a factor in bringing about cell changes which invite cancer. The genitalia in men undergo no such sudden and profound senile changes; inasmuch as the testis is the primitive organ of procreation from which the ovary is derived, it has a protective heredity behind it.

It is worth while occasionally to go back and take account of stock, so to speak, to see what we really know about cancer that has stood the test of time.

We have thought of cancer so much in relation to the human being that we have not always kept clearly in mind that every living thing may suffer from an analogous disease. The late Dr. Erwin F. Smith, working in the government laboratories in Washington, found that cancer in plants had the essential characteristics of cancer in man, and he noted the relation of these types of plant tumors to certain bacteria which he believed to be the cause either of such cancers or of irritation in susceptible plants which resulted in those changes in cells which were responsible for the tumors.

The development of cancer in the lower animals has received a greater amount of study than cancer in plants, and is fairly well understood. The disease in the lower animals, again, exhibits the same general characteristics as in man: that is, cell changes, growth to the limit of obtaining blood supply, and transplantability in the same animal through metastatic processes, with which we are only too familiar.

Cancer does not appear in sound tissues. Investigation of the various theories of the causation of cancer shows that the one provocative agent which remains unchallenged is chronic irritation. In all lands, among all peoples, we see this one causative influence in the ascendant. In China, among those who shave their heads with a dull and rough-edged razor, cancer of the scalp is common, but does not occur among those who do not shave the scalp. The Chinese men eat at the first table, when the rice is hot, throwing it with some force by means of chopsticks into the mouth and pharynx, and not infrequently they suffer from cancer of the pharynx and the beginning of the œsophagus. The women, who eat at the second table, when the rice is cold, seldom have the disease. In Australia the sharp-edged sand in the desert portion of the country, blown by the hot wind, so frequently produces cancers of the skin of the face that such cancers are called the "Australian disease." In certain parts of India and the Philippines, where the betel nut wrapped in its leaf with lime is chewed, cancer of the mucous membrane of the cheek is still common. Among smokers, cancer of the lip sometimes develops, less commonly since heat-conducting clay pipes are no longer used. Cancer of the gums and about the teeth is less common now that by modern methods of dentistry irritating stumps and roots may be removed. Cancer of the breast occurs largely among civilized women. In those countries in which the breasts are allowed to be exposed, that is, are not compressed or irritated by covering, it is rare. In the mountain regions of Kashmir, India, where the people carry braziers filled with hot coals strapped onto the lower part of the abdomen, cancer just above the pubis is common.

With improvements in construction of buildings and change in fuel, there are no longer many chimneys which require cleaning, so that chimney-sweep's cancer of the groin is less common, but we still see an occasional cutaneous epithelioma on the shins of railroad engineers and firemen whose legs have been exposed during years to the intense heat of the engine fire-box.

I have merely touched on these few outstanding examples of cancer of visible parts of the body about which there is little dispute. As to cancer of the interior of the body we have less definite proof, but cancerous gall-bladders usually contain stones, and that ulcer of the stomach may be responsible for cancer of the stomach is admitted by all, although there are great differences of opinion as to its frequency. Hurst has given statistics to show that in about 20 per cent. of cases of ulcer of the stomach, cancer may be expected. In our own experience, while the percentage in which the histologic examination of excised cancers of the stomach for evidence of preceding ulcer varies in different series of cases, the development of gastric cancer on some type of demonstrable precancerous disease such as ulcer is present in more than 25 per cent.

Cancer of the stomach in men constitutes a third of the total number of cancers in all parts of the body. The cause of the greater frequency of cancer of the stomach among men has not been solved. The men of the

racers that do not confine themselves to civilized customs are less often affected by cancer of the stomach. Do hot drinks change the gastric epithelium, or does food in large quantities wear out its secretory function so as to produce premature changes in the gastric epithelium? Cancer of the small intestine is rare as compared with cancer of the stomach, large intestine and rectum, which have a short heredity as compared with the primitive small intestine, and this may be a factor.

When we try to estimate the exact relationship of sources of chronic irritation to cancer, there are various explanations. Certain observers believe that the site of chronic irritation, unprotected by normal epithelium, permits the entrance of an outside agent, perhaps a microörganism, but if so, why should the metastatic process always show the histopathologic characteristics of the original lesion? A metastatic process in the liver from a cancer of the gastro-intestinal tract shows, not cancer of the liver, but a secondary cancer of the gastro-intestinal epithelium in the liver.

A possible explanation is that when the tissues have been subjected to a long-continued insult, the reparative processes are exhausted and, instead of healthy cells, less mature cells are thrown into the breach of continuity until finally embryonic cells are used to replace the normal epithelium.

New revelations would make it appear that cancer may be the result of agencies acting from within the body due to biochemical dysfunction affecting the life history of embryonic cells. In any event, it may be assumed that the agents which act on the cell to produce malignancy become an inseparable constituent of the cell, as metastasis takes place only by the transplantation of the malignant cell itself.

Individuals vary in their susceptibility to the cause or causes of cancer, whatever they may be. In no other way can we explain why 90 per cent. of persons do not have cancer, and why 10 per cent. of them die from it. It is as logical to accept the hypothesis that the 90 per cent. of persons have greater resistance to cancer than the 10 per cent., as to attempt to force an explanation of why only 10 per cent. come in contact with hypothetic causative agents. If the patient's susceptibility to the disease is the significant factor in the development of cancer, the site of the growth would be determined by the tissue or organ subjected to the insult of a precancerous lesion, and the grade of malignancy and the metastatic possibilities by the susceptibility of the body as a whole. Perhaps the reason cancer usually appears after middle life is that the cells of the body have lost the reparative power of youth, have a lessened immunity, and thereby have become more vulnerable.

Certain sources of chronic irritation seem to have greater potentiality to produce malignant disease than others, such as unrefined tar, which seems to possess more than ordinary powers of precancerous irritation for susceptible animals.

The local response of the tissue subjected to chronic irritation apparently is influenced by general systemic factors which may either accelerate or delay the development of cancer. Murray's work leads to the inference that there

## SUSCEPTIBILITY TO CANCER

are variations in the resistance or, conversely, in the susceptibility of individual mice to cancer from tar painting. Slye found that by breeding strains of mice in which the disease developed most readily, the susceptibility of these strains could be increased enormously, so that mice would be born with the disease. By mating mice that were not so readily susceptible to cancer, strains could be developed in which cancer could not be produced and to which cancer could not be transferred.

The malignant cell has a remarkable resemblance to the rapidly growing embryonic cells of the chorionic villi (Langhans' cells). The stroma of a cancerous growth is the measure of nature's resistance. The greater the amount of stroma and the less the proportion of cells, the slower the growth. Wilson, MacCarty, and Broders have enlightened us greatly with regard to the histologic character of the cell in relation to malignancy. Wilson was able, twenty-five years ago, to develop an original polychrome methyl blue stain for frozen sections which gave good differential coloration of the various elements of the cell, thus making possible an immediate microscopic diagnosis. MacCarty called attention to the significant fact that the greater the proportion of the nucleus and the less the differentiation of the cell cytoplasm, the more rapid the growth of cells; that an excess of the nucleolar element is associated with the type of rapid growth and invasion which is clinically malignant. Broders, in a careful clinicopathologic study of the relative amounts of cell differentiation in a tumor, pointed out that the more nearly the cancer cell approaches normal, the less the malignancy, and was able to develop an index of malignancy. Bowing found from experience with radium and X-ray that the more severe grades of cancer, Grades 3 and 4 of Broders' classification, may sometimes be made to take on the more favorable aspects of the cancers of Grades 1 and 2, with definite slowing of the process, so that sometimes such a lesion primarily inoperable may become operable.

The assumption has always been that the more severe grades of cancer are due to a more potent cause. I hardly need point out that these newer revelations throw some doubt on so ready an explanation. It is equally, if not more, probable that the more severe forms of cancer and the development of cancer in certain tissues are due to increased susceptibility.

The foregoing studies logically lead to the idea of increasing individual resistance to the disease and its ultimate prevention. Science has been able to develop soil changers in smallpox, diphtheria and tetanus. Why not in cancer? Because of natural immunity to the disease relatively only a small proportion of the total population is susceptible to scarlet fever. With the Dick test the degree of natural immunity of the individual to scarlet fever can be determined, and if it is not sufficient to protect from the disease, it can be increased to normal by serum. Why not in cancer? Perhaps the development of cancer as well as its degree of malignancy is attributable to the diminished activity of immunizing processes rather than to the nature of the activating agent.



# RESISTANCE AND SUSCEPTIBILITY TO CANCER

By W. CRAMER, M.D.

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FROM THE IMPERIAL CANCER RESEARCH FUND

WHEN the experimental production of cancer by painting with tar or other carcinogenic agents had been developed as a laboratory method, so as to yield positive results in practically 100 per cent. of the tar-painted animals, it was demonstrated beyond doubt that cancer was at its inception a local disease which arose in a limited area of cells subjected to chronic irritation. It was natural that at first the attention of workers in this field was riveted upon the *production* of cancer and that most of the work was designed so as to induce cancer as rapidly as possible and in the greatest number of animals subjected to the experiments. This could be obtained by applying tar as frequently as possible consistent with the survival of the animals, by applying tar to a relatively large area of skin and by continuing the application of tar to each animal until a tar cancer appeared.

*Experimental Demonstration of Resistance.*—If, however, the opposite device is adopted (that is to say, if tar is applied to as small an area of skin for a limited period of time and with a frequency just sufficient to induce cancer with a fair degree of regularity in a certain percentage of the experimental animals), quantitative differences are revealed in the reaction of different individual animals to tar painting, which are of considerable significance. The results of a typical experiment of this kind will make the meaning clear. In this experiment 100 female mice aged from three to six months were subjected to the repeated application of an actively carcinogenic tar preparation. The preparation used is one which had been kindly placed at our disposal by Professor Passey. A drop of tar was applied twice weekly to the epilated skin between the shoulder-blades. This was continued for four months. After that period no further tar was applied to any of the mice, which were allowed to complete the natural span of their lives. As soon as warty growths appeared, they were entered on charts and when a growth was considered to have become malignant, it was removed by operation and the diagnosis verified by microscopic examination. One object of this procedure was to determine the onset of malignancy as accurately as possible. It was unavoidable that in a few cases tar tumors were excised which on microscopic examination proved to be of doubtful malignancy. There was a massive hyperplasia and downgrowth of the epithelium, but no clear evidence of infiltrative growth. Such tumors, which were, fortunately, only five in number, are not classed among the tar cancers. In addition to the mice which developed tar cancers of the skin, there were those which developed papillomata which remained in that state until the death of the animal. A third group of negative mice remained without any growth whatever until their

death. When the mice died any growth present on the skin was examined microscopically and search was made for the presence of metastases or of neoplasms on other parts of the animals. In such an experiment one obtained therefore three groups of animals, which will be called: (1) The cancer group; (2) the papilloma group; (3) the negative group. These will now be discussed separately.

(1) *The Cancer Group*.—Table I and Fig. 1 give the number of mice which developed tar cancer in each month reckoned from the beginning of tarring (December, 1927). The total number of mice with tar cancer is fifty-one. The first two tumors appeared at the end of the fourth month just at the end of the course of tarring. One of these two tumors appeared at once as a malignant growth, and, although excised as soon as it had been noticed, metastases developed in the axillary glands one month later. The number of tar cancers showed a rapid increase and reached a maximum in the sixth and seventh months. This was followed by an equally rapid decline in the following months. The last tar cancer appeared one year and one month after the beginning of tar painting.

Only two mice developed recurrences at the site of tar painting. The recurrences are not counted in the number of mice with tar tumors, although, in view of the wide excision practiced with every tar cancer, they most probably represented new tumors.

As already stated, the tar cancers were removed by operation as soon as their malignancy was recognized. The animals of this group of "surviving cancer mice" died during the following year, mostly from intercurrent disease, or, more rarely, from metastatic growths in the lungs. If metastatic growths appeared in the axillary glands, they were removed by operation. It is interesting to note that the survival in the group of "cancer mice" was longer than in the "negative group." Thus, one year after beginning of tar painting there were, alive, thirty mice of the fifty-one mice which had developed tar cancer and only ten mice of the forty-nine mice which had shown neither warts nor tar cancer. Moreover, some of the operated surviving cancer mice were still alive in the third year of the experiment, while the last mouse of the negative group died twenty months after the beginning of tarring. Such a result lends no support to the view that in the induction of cancer by tar painting a "toxic" effect of the absorbed tar on the whole organism plays an important part.

(2) *The Papilloma Group*.—This group need not be discussed in detail, as all the animals of this group which survived the first year of the experiment had developed malignant tumors. There remain only the five mice mentioned above from which tumors had been removed as malignant new growths, which, on microscopic examination, proved not yet to have reached the stage of malignancy. They are therefore eliminated from the experiment. These five mice were alive at the end of the first year and remained negative during the second year, when they died.

(3) *The Negative Group*.—This group shows a gradual diminution as

the experiment proceeded, as the result either of the animals' developing tar cancer or of death from intercurrent diseases. Of this group ten mice were still alive at the end of the fifteenth month. They remained negative during the second year of the experiment, the last mouse dying twenty months after the beginning of tarring.

*Results.*—The actual data are given in Table I and represented graphically in Fig. 1. Using age periods of one month after beginning of tarring, the

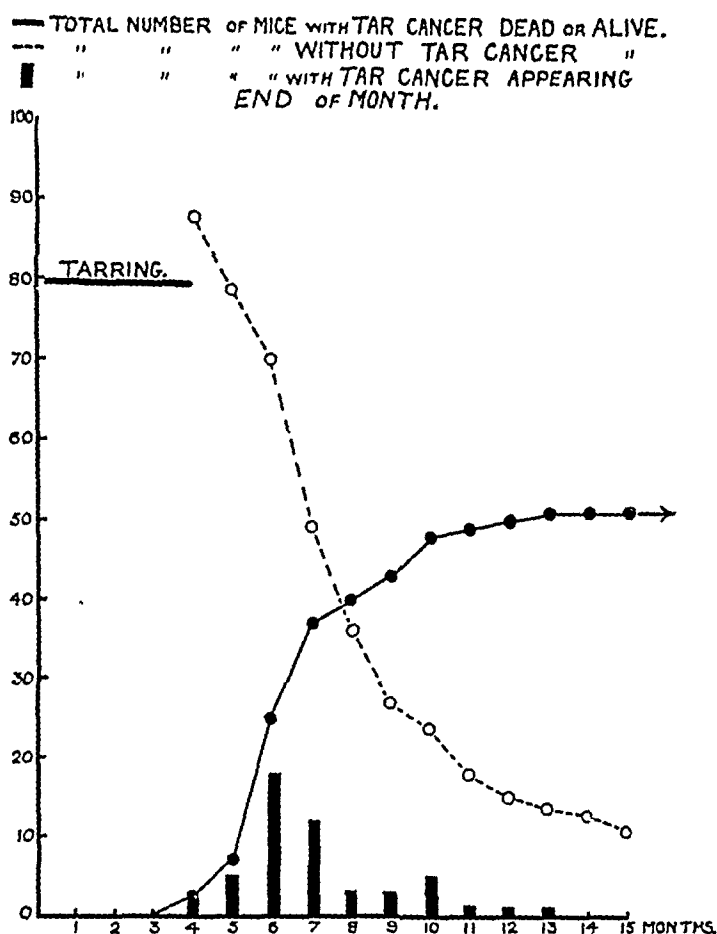


FIG. 1

figures given are: (1) The number of mice developing a tar cancer in each age period, and (2) the number of surviving non-cancerous mice for each age period (*i.e.*, papilloma group + negative group). From (1) and (2) it

TABLE I

| Months from Beginning of Tarring                    | 4   | 5   | 6    | 7    | 8   | 9    | 10   | 11  | 12  | 13  | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
|---|-----|-----|------|------|-----|------|------|-----|-----|-----|----|----|----|----|----|----|----|
| Tar Cancers Appearing at End of Month               | 2   | 5   | 18   | 12   | 3   | 3    | 5    | 1   | 1   | 1   | 0  | 0  | 0  | 0  | 0  | 0  | 0  |
| Non-cancerous Survivors.....                        | 88  | 79  | 70   | 49   | 36  | 27   | 24   | 18  | 15  | 14  | 13 | 10 | 6  | 3  | 3  | 1  | 0  |
| Percentage of Tar Cancer in Non-cancerous Survivors | 2.3 | 6.3 | 25.7 | 24.5 | 8.3 | 11.1 | 20.8 | 5.5 | 6.6 | 7.1 | 0  | 0  | 0  | 0  | 0  | 0  | 0  |

## RESISTANCE AND SUSCEPTIBILITY TO CANCER

is possible to calculate for each age period the percentage of non-cancerous mice which developed cancer. This is given in the lowest column of Table I and represented graphically in Fig. 2. It is necessary to elaborate these points in order to exclude the possibility that the marked decline in the appearance of tar cancers after the seventh month was due to a high death rate among the non-cancerous survivors. Fig. 2, which gives the percentage of tar cancers developing in each month in the group of non-cancerous survivors, shows that the percentage after having reached a maximum of 25 per cent. during the sixth and seventh months gradually declines to the zero line, indicating that the surviving mice remain free from cancer. In an experiment with continued tarring in which the surviving negative mice continue to be sub-

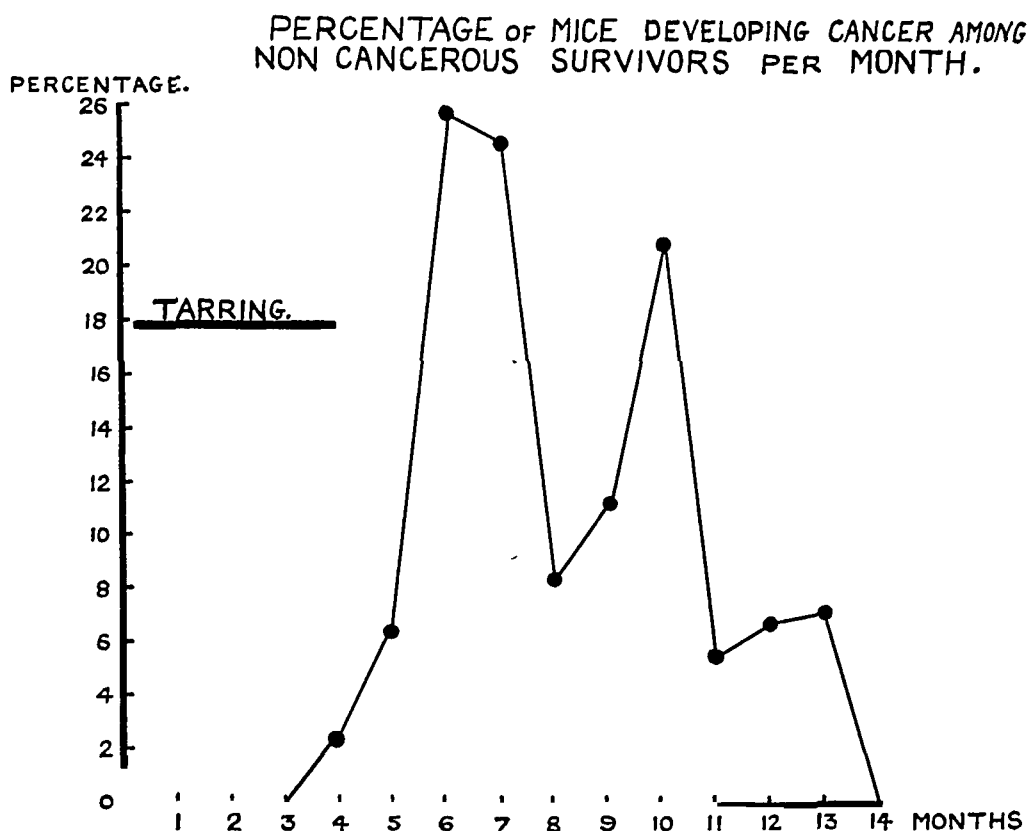


FIG. 2

jected to tarring until they also develop tumors, the curve representing the "total number of mice with tar cancer, dead or alive" shows a continual rise up to the end of the experiment, and so does the curve representing the percentage incidence of cancer in the negative survivors, while the curve representing the negative survivors shows a continued fall and eventually reaches the zero line, when all the surviving mice have developed a tar cancer.

The experiment with limited tarring shows conclusively that a degree of chronic irritation which is sufficiently severe to induce cancer in the majority of the tar-painted animals within the usual length of time (six or seven months) will show a greatly delayed carcinogenesis in a smaller group and will even leave a definite proportion free from cancer. Carcinogenesis by chronic irritation is therefore dependent upon a factor—or a group of factors

—which may be conveniently designated by the term “susceptibility,” or, if one uses a reciprocal term, “resistance.”

This phenomenon is of constant occurrence. Thus, in two further series of experiments on a smaller number of animals, mice were subjected to painting with the same actively carcinogenic tar preparation for four months. In each series fifty mice were treated in this way. On the thirteenth month after the beginning of tar painting the results were as follows:

|                   | Carcinomata—<br>Dead and Alive | Papillomata—<br>Dead and Alive | Negative<br>Survivors |
|-------------------|--------------------------------|--------------------------------|-----------------------|
| First group.....  | 11                             | 4                              | 6                     |
| Second group..... | 5                              | 2                              | 4                     |

Reference may be made here also to an experiment carried out by Dr. R. J. Ludford (1929) in this laboratory and published recently. In this experiment, which was designed to study the effect of scarification on the induction of cancer by tar painting, two control series were made. In one, tarring was carried out for three months only; in the other, tarring was continued for each mouse until a papilloma appeared. The same tar preparation was used (Passey Tar). Twenty-five mice were tarred in each group. The results after the thirteenth month were as follows:

|                            | Carcinomata—<br>Dead and Alive | Papillomata—<br>Dead and Alive | Negative<br>Survivors |
|----------------------------|--------------------------------|--------------------------------|-----------------------|
| Continued tarring.....     | 8                              | 5                              | 0                     |
| Three months' tarring..... | 8                              | 1                              | 4                     |

In this experiment, continued tarring produced not only 100 per cent. of tumors, but the tumors appeared much sooner than in the group submitted to limited tarring.

It may be argued that in the mice subjected to limited tarring, the negative survivors would also develop cancer if they lived long enough. In our experiments, the negative surviving mice died without having developed cancer when they had reached an age of about one and three-quarters to two years; that is to say, they were middle-aged to old mice. They died from the natural risks to which the life of a mouse kept in laboratory conditions is subject. Even if it be admitted for the sake of argument that these mice would develop cancer if they could be kept alive long enough, the fact would remain that there are individual mice in which the onset of cancer is so greatly delayed that death occurs late in life from other causes, while in others cancer develops with comparative rapidity.

*Anatomical Site of Resistance.*—The factors which determine “resistance” or “susceptibility” may reside in the epithelial cells themselves, or they may be in the skin tissue as a whole, or they may reside in the organism as a whole. These possibilities, which do not mutually exclude each other, are capable of experimental investigation.

There is experimental evidence that the development of tar cancer can be influenced by conditions operating on the whole organism. Thus Maisin and

his collaborators (1923, 1925) have shown that the induction of cancer in mice by tar painting can be accelerated by the injection of tar at a site remote from the tarred area. A similar acceleration has been observed by me (1926) in experiments on mice in which the spleen had been removed, minced and reintroduced intraperitoneally into the splenectomized mice. There are also peculiar features of the incidence of cancer in man which indicate the existence of systemic factors influencing the development of malignancy. Thus, in occupational cancer the disease develops only in a fraction of the individuals exposed to the chronic irritation induced by the occupation. What is more, some individuals may develop cancer although they have been engaged in the particular occupation for a few years only, while others, who have followed the occupation all their lives, remain free from the disease.

In the last two Annual Reports of the Imperial Cancer Research Fund, J. A. Murray (1928) and W. Cramer (1929) have discussed the bearing which international cancer statistics have on this point. The following figure, which is reprinted from the Twenty-seventh Annual Report of the Imperial Cancer Research Fund, shows that, while the recorded total incidence of cancer in the women of different countries is approximately the same, the recorded organ incidence varies

greatly. It is even more remarkable that if a similar comparison is made for men and women of the same country, the same relationship is found. One must either dismiss these facts as a mere accidental coincidence, or one must attribute them to an underlying, systemic factor.

It is agreed that cancer develops as a result of chronic irritation. Cancer

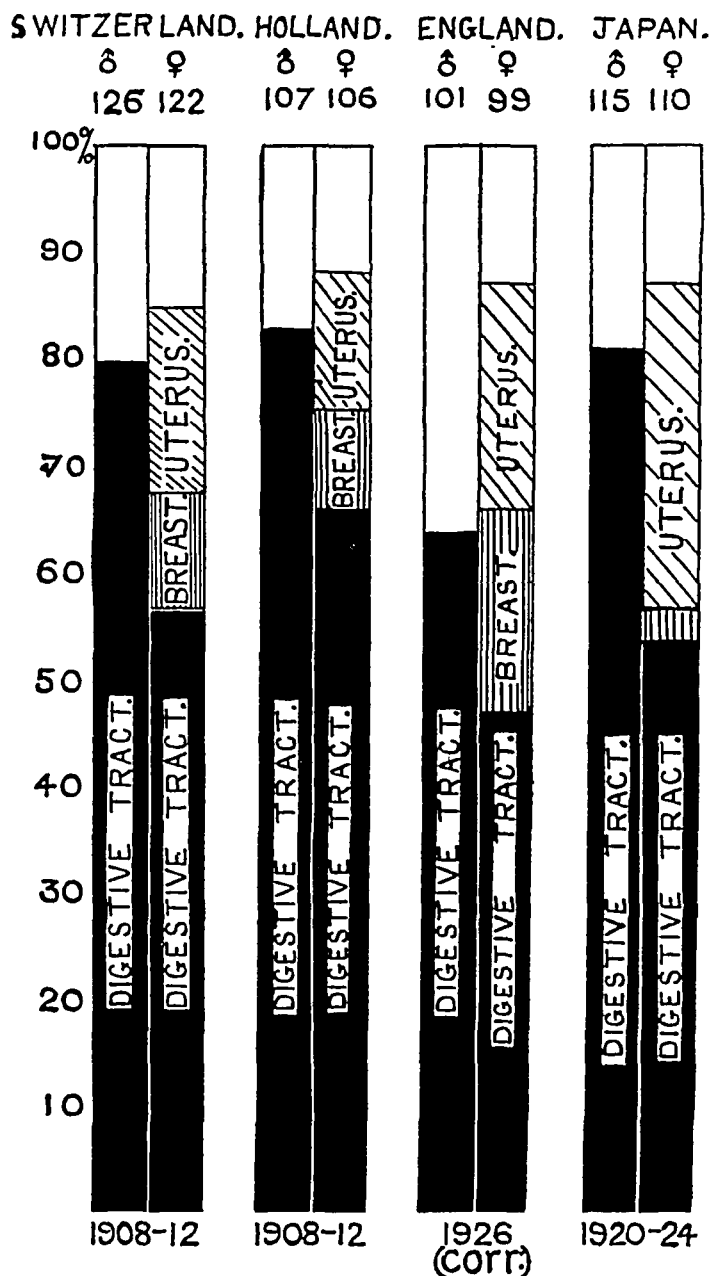


FIG. 3.—Comparison of the organ distribution of cancer in males and females in four countries. The line of figures at the top of the diagram gives the crude annual death rate per 100,000 living of each sex (except for England, for which the corrected rate has been taken). Reprinted from the Twenty-sixth Annual Report of the Imperial Cancer Research Fund.

will therefore arise most frequently in those organs which are most exposed to chronic irritation. These organs are, in men, the digestive tract; in women, the digestive tract, the mamma and the uterus. They account for about 75 per cent. of all cancer cases. It has been assumed hitherto that the incidence of cancer in man is determined entirely by the incidence of chronic irritation; that is to say, that when cancer develops in an organ of an individual, it is because that organ has locally been subjected to a certain amount of chronic irritation. That is, broadly speaking, true. But it does not follow—and in the light of our experiments it is not true—that the same degree of chronic irritation would produce cancer in other individuals. The experiments on mice given above have shown that the degree of chronic irritation necessary to induce cancer varies for different individuals, so that a degree of irritation sufficiently severe to induce cancer in some individuals will leave others free from the disease. The difference between an individual suffering from cancer and one free from cancer may be due to the fact that the former has been subjected to a more intense degree of chronic irritation than the latter. But it may also be the case that the degree of irritation was approximately the same but that there was a difference in the individuals subjected to it, the former reacting to it more readily by the development of malignancy than the latter. The incidence of cancer in man is therefore determined not only by the one extrinsic factor—the incidence of chronic irritation—but also by the intrinsic factor—susceptibility or resistance of the individuals whose organs are being subjected to chronic irritation. When, therefore, a comparison is made between the incidence of cancer in men and women of the same country, it must be borne in mind that in women there are three organs (mamma, uterus, digestive tract) which, being most exposed to chronic irritation, will pick out those individuals in which cancer develops most readily—the susceptible individuals—while in men there is only one—the digestive tract. This is sufficient to account for the fact that in men the incidence of cancer falls more frequently on the digestive tract. And since the total incidence of cancer is about the same for men and for women, although the organ incidence differs widely, the conclusion seems justified that the factor which determines the susceptibility to cancer of one organ is the same for the other organs.

Similarly, if a comparison is made between the incidence of cancer between the women of different countries, different habits of life will vary the degree of chronic irritation to which the organs in question will be subjected. Thus, if the habits of life in one country are such as to increase the processes of chronic irritation in the digestive tract as compared with another country, a larger number of susceptible women will develop cancer of the digestive tract and, therefore, fewer susceptible women will remain to develop cancer of the breast and uterus. This example accounts for the fact that Dutch and English women have an equal total incidence from cancer but a very different organ incidence.

The possibility that factors of susceptibility or resistance reside locally in

the tissue subjected to chronic irritation was investigated by the following experiment.

A *large* area of skin was subjected to tar painting for a limited period, and any cancer which arose was removed by operation as soon as its malignancy was recognized, leaving behind the remainder of the tarred area. The results have already been published in detail (Cramer, 1929), so that they need be only briefly reviewed here. It was found that the appearance of the first malignant tumor was almost always limited to one centre. Even if the tarring was followed by the appearance of multiple papillomata, the malignant development occurred in only one of them, or in two closely neighboring ones. It was rare to find two carcinomata developing from two distant centres. After removal of the first cancer, a second cancer frequently developed after an interval varying from several weeks to several months. Under favorable circumstances—that is to say, if the mouse lived sufficiently long—the removal of the second tar cancer was sometimes followed by the development of a third tar cancer. In one case, a year and a half elapsed between the beginning of malignancy and the development of the second tar cancer. These experiments show, therefore, that the skin of one mouse may exhibit differences in susceptibility to tar cancer similar to those shown by different individual mice. It is clear, therefore, that some of the factors which determine resistance reside in the tissue itself.

The next question is whether variations in the susceptibility of a given tissue—in this case the skin—are determined by the epithelial cells or by the connective tissue, including in this latter term blood and nerve supply. The most obvious and most generally accepted conception of carcinogenesis is that the process is determined entirely by changes in the epithelial cells. If that were the case, differences in susceptibility would have to be referred to differences in the epithelial cells themselves. One would then have to make the *ad hoc* assumption that the skin epithelium is a mosaic of cells of a different inherent constitution. Carcinogenesis by tar painting of a small area would thus become a lottery, the result depending on whether the small tar-painted area happens to include a susceptible cell or not. The same would hold good for the development of cancer in man. The regularity with which experimental tar cancers develop with this technic is against such a view. Moreover, if this view were correct, negative results should be largely eliminated if a large area is subjected to tarring, since, under these conditions, the possibility of missing susceptible cells is excluded as much as possible. The technical difficulty here is that in the tarring of a large area more tar is absorbed, so that a toxic effect is produced on the animals and few mice survive the procedure. If one restricts tarring of a large area to tarring once a week, one finds again some mice surviving nine months without developing tumors, while the bulk of the animals has responded by the appearance of carcinomata or papillomata. Another experimental method of testing this question is the application of trauma to the epithelial cells. Deelman (1927) stated that persistent traumatization of the skin from outside, which stimu-



lated regeneration of the epithelium accelerated carcinogenesis by tar painting. Most observers have been unable to confirm this observation (Roussy, Leroux and Peyre, Ludford, Cramer). Ludford (1929), in the paper mentioned above, found that when scarification preceded tar painting, carcinogenesis was slightly retarded, and that when scarification followed tar painting carcinogenesis was inhibited almost completely.

But when a trauma is applied to the tarred skin from below—that is to say, when it is applied to the connective tissue—it has been possible in a number of cases to elicit carcinogenesis in a papilloma. Conversely, the inhibition of carcinogenesis by scarification, observed by Ludford, was attributed by him to the sclerosis following scarification.

The idea that the connective tissue plays an important part in the development of malignancy is not a new one. The experimental study of carcinogenesis has shown that, in the development of a carcinoma, changes take place not only in the epithelial cells, but also in the underlying connective tissue. Quite recently, Kreyberg has made an important contribution by demonstrating a well-defined series of vascular changes in the connective tissue of the tarred area, preceding the development of cancer. It is clear that a definite relationship must exist between the non-malignant epithelial cell and the connective tissue, and that this relationship is altered when the epithelial cell has become malignant. This is merely a restatement, in other words, of the fact that in regeneration and in benign hyperplasia the cells remain within the normal bounds set by the connective tissue, while in a malignant hyperplasia they invade it. Another experimental demonstration of this relationship is given when epithelial cells are transplanted from one animal to another. Both the malignant cell and the non-malignant cell elicit a reaction in the connective tissue. But with the non-malignant cell, this leads eventually to the destruction and removal of the implanted cells, while the malignant cell is able to dominate the reaction so as to compel the formation of a stroma which enables the implanted cells to live. Murray and Woglom (1921), in their investigations on experimental tar cancer, concluded that “progressive growth of autoplasts is proof of the cancerous nature of the growths which show it, even though, histologically, they may seem to be innocent.”

A further example of the importance of the relationship between malignant cells and the stroma is afforded by the study of regressing tumors: Woglom (1922) has shown that regression may occur in a spontaneous, malignant new growth, the cells of which are still alive and even actively undergoing mitosis. He states that “a retrogressing carcinoma may be indistinguishable under the microscope from one that is increasing in size, or it may be totally keratinized or largely necrotic.” Similarly, the external application of radium may bring about the regression of a malignant tumor by a process closely resembling that involved in the spontaneous regression (Cramer, 1905, 1928). The cells of a regressing, transplanted tumor can be inoculated successfully into other animals, although with a low percentage of “takes” (Bashford,

Murray and Bowen, 1908). Similarly, the cells of a tumor which has received a dose of radiation sufficient to induce complete regression can be transplanted with a high degree of success into other animals, if the irradiated tumor is removed within a few days after radiation (Mottram, 1927). Further, one transplanted tumor can undergo regression while another tumor continues to grow in the same animal. Neither a change in the malignant cells alone nor a general reaction on the part of the organism can account for these phenomena. They can only be attributed to a local change in the relationship between the malignant cells and the stroma. It is possible to define exactly the part played by it in carcinogenesis. But there is a good deal of circumstantial evidence that in the transformation of hyperplastic epithelium into malignancy the connective tissue plays an important part and may be responsible for differences in susceptibility to cancer. Since the connective tissue pervades the whole organism and since its activity is subject to conditions imposed by the organism, it is possible to understand how susceptibility could be influenced both by local conditions and by the organism as a whole.

## SUMMARY

Generally speaking, the experimental analysis of the process of carcinogenesis shows that this process is one which does not arise merely as the result of a direct action of a carcinogenic agent on epithelial cells, as is generally supposed, but that it is a much more complex one. In one sense, it emphasizes the local origin of the disease, for even if a large area of epithelial cells is subjected to chronic irritation, cancer arises only in a very small portion of this area. In another sense, it widens this conception by showing that the local development of malignancy is influenced by factors which do not reside in the epithelial cells but in the organism, and exert their activity presumably through the mesenchymal cell system. The terms "susceptibility to cancer" or "resistance to cancer" are intended to embrace the activity of these factors. The practical importance of these considerations lies in the possibility that the study of these factors may enable us to modify their activity in such a way as to delay, or even to prevent, the onset of cancer.

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# HEREDITY AND CANCER

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WHEN physicians who have been for years and years in practice are asked whether hereditary factors are of any influence on the development of tumors, the answer is, in this country, usually in the affirmative. This is merely an impression, but an impression which has a value in the case of a disease which is so frequent as cancer. The frequency of cancer is higher in Holland than that of tuberculosis. The tuberculosis mortality decreases every year, while the mortality rate of cancer is constantly increasing. With Denmark and Switzerland, Holland has the doubtful privilege of being at the head of a series of countries with the highest cancer mortality rate.

When actual facts which support the assertion just made are asked for the answer is generally unsatisfactory. From time to time a family is met with which is said to be a cancer family, but of the behavior of cancer in general with respect to hereditary factors our knowledge is very slight. There are a great many questions connected with this subject for which no solution has been found. I might mention one of these. If hereditary factors really are of influence on the development of tumors, there are two possibilities. Either the influence is a direct one, or it works indirectly, by way of the heritability of forms and functions of organs and systems. It is possible to imagine that a colon which is too long and a bad functioning of the stomach are hereditary conditions and that these abnormal conditions are of fundamental significance for the etiology of tumors. We are familiar with the same fact in tuberculosis. The form of the thorax may be a hereditary factor, the outbreak of the illness a direct consequence of this form.

In the field of human cancer study we have hitherto had to be content with few facts. The study on the experimental basis—such as Miss Maud Slye has carried out on mice—is much more hopeful. Nevertheless, research work on human material must be continued. In Holland, Doctor Wassink, the director of the Dutch Institute for Cancer Research in Amsterdam, published a study on this subject some years ago. He utilized the data which the patients who visited the institute were able to give him about the occurrence of cancer and other tumors in their family. The most important result of his study was that for some forms of cancer, hereditary factors could be demonstrated. For instance, in the case of cancer of the breast and cancer of the uterus, the occurrence of the same form of tumor in the family of the patients is much more frequent than would be expected from the annual statistical publications. For other forms of cancer this could not be established. For example, in the case of cancer of the buccal cavity, this form of tumor in the family of patients suffering from this growth was not more

frequent than statistics would suggest. As to how cancer in general is related to family disposition, and particularly how cancer of the stomach—the most important form of cancer—behaves in this regard, the material of the Amsterdam Institute was insufficient. The question I put myself was the following: Is cancer in general in the family of cancer patients more frequent than in any other family in which there is at this moment no cancer patients? To my mind it is not advisable to inquire of the patients themselves as to their family data; it seems more likely to be successful to inquire of the physicians under whose treatment the patients are or have been. I therefore invited the collaboration of the physicians of the two northern provinces of the Netherlands, namely Friesland and Groningen. It may be supposed that during the illness of a cancer patient, or after his death, the physician has an opportunity of consulting the relatives about the appearance of cancer in the patient's family in former years. Physicians who have been for years and years in the same practice know something themselves about the family of their patients. I made another request to the physicians, namely

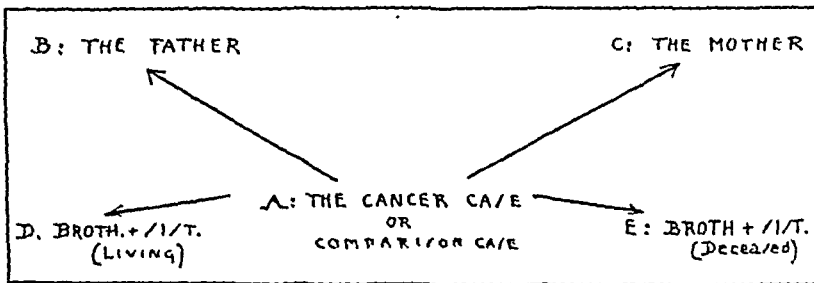


FIG. 1.

that they should send me along with the data regarding the cancer patient, the same data about any patient *not* suffering from cancer. They were asked to collect this data in precisely the same manner as the cancer data. Thus two series of family data were obtained. First, the data regarding the cancer patients; secondly the same about non-cancer patients of the same age. It is necessary to make the following remark concerning the coöperation of the physicians. In the northern parts of Holland, with their prosperous population, which has a firm belief in medical science and its representatives, the contact between physicians and patients is an intimate one. In the southern parts of this country this is not the same. Research work such as I mentioned above I consider to be possible only in the northern parts and especially in the country districts with a settled population. The urban population is useless for this purpose. At any rate, the data collected in this way are more reliable than information that patients can give themselves as to their relatives.

The forms which were sent to the physicians were arranged as follows: At A are placed the data regarding the cancer patient (or the comparison case).

At B and C we find the data regarding the parents of the cancer patient. At D, the data regarding the brothers and sisters who were still living, and at E what was known about their deceased brothers and sisters. In this

way data were collected regarding 350 cancer cases and about 250 comparison cases. It was found in practice to be difficult to furnish a comparison case for every case of cancer. The number of the former is, therefore, smaller than that of the latter.

First of all it is necessary to decide whether it is admissible to compare the two series of data received from the physicians. This was found to be actually the case. The ages of the two series of patients were the same. The same applies to the number of members of the families. This is an important point. In the two series of cases the number of brothers and sisters—both living and deceased—was equal. Moreover, the average ages in the two series were also the same. In such research work the unknown causes of death form a large group; more especially in the case of the parents, who died

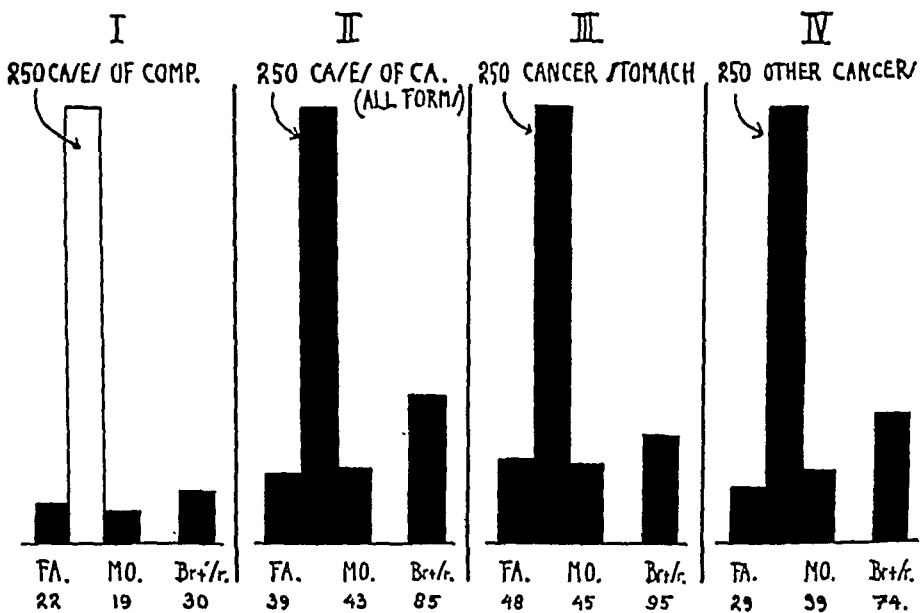


FIG. 2.

long ago, the unknown causes of death are a large category. We found in both cancer and comparison cases 21 per cent. of unknown causes of death. Thus in this direction the two groups of data were identical.

Here follow some of the figures as derived from the material. For the convenience of the reader I have drawn some diagrams in which the data are arranged in an easy manner. The cancer group is divided into two categories: cancer of the stomach and all the other cancers together. All the data are calculated for groups of 250 cases. Comparison is therefore immediately possible. In the first diagram are four sections. The first one (I) refers to the cases of comparison. The long blank strip represents 250 cases of comparison. Immediately to the left of this are placed the cancer cases which were found among the fathers of these 250 cases. Immediately to the right are placed the cancer cases among the mothers. Farther to the right will be found the cancer cases among brothers and sisters. The second figures (II) is the same grouping of 250 cases of cancer in general (black

## HEREDITY AND CANCER

strip). The third one (III) is the same for cancer of the stomach and the fourth one (IV) refers to the cancer of all the other organs together.

In the group of cases of comparison (I) we found in 250 cases 22 cases of cancer among the fathers, 19 among the mothers and 30 among the brothers and sisters. In total in 250 cases of comparison we found in the family  $22+19+30=71$  cancer cases. For the second group (II) (cancer in general) we found the following numbers: among the fathers of 250 cancer cases, cancer as a cause of death occurred in no less than 39 cases, among the mothers 43 cases, among the brothers and sisters in no less than 85 cases. In total among 250 cancer cases we found in the family  $39+43+85=167$  cases of cancer. *In the cancer cases we found cancer more than twice as*

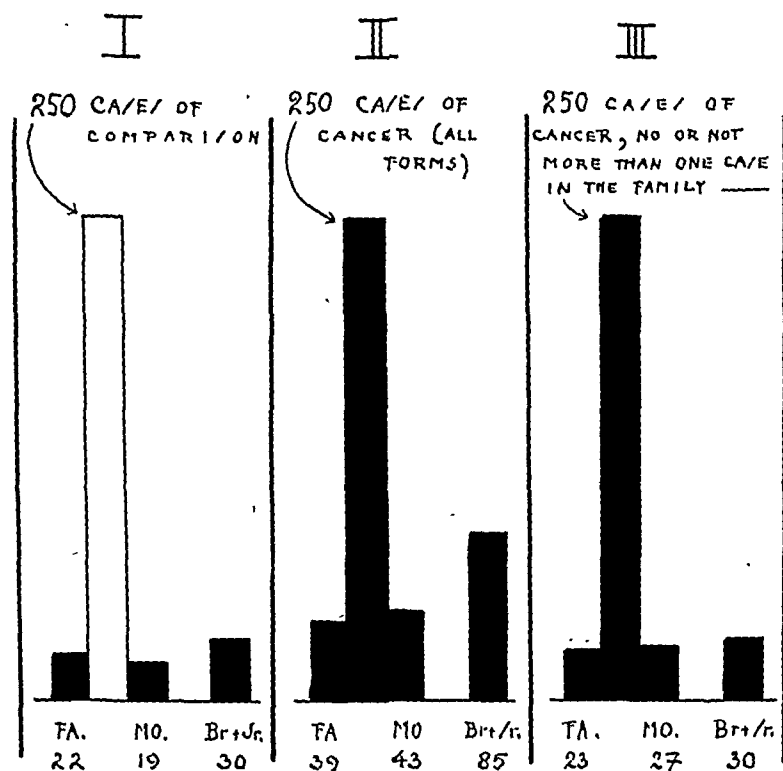


FIG. 3.

frequently among the parents as in the cases of comparison; in the group of brothers and sisters three times as frequently. For cancer of the stomach (III) and cancer of other organs (IV) we found the same differences as compared with the non-cancer series. For cancer of the stomach this difference was still more marked. The numbers are to be found in the diagrams III and IV.

The conclusion that can be drawn so far is this: Cancer is more frequent in the family of cancer patients than in any other category of families in which at the moment there are no cancer patients. The differences are more marked in the group of brothers and sisters than in that of the parents of the patients.

Many questions now arise. Among other things it would be interesting to know how cancer of different organs behaves in this respect. I did not wish to go farther than cancer of the stomach. The categories of other

organs were too small for analysis. We hope to do this in some years when the material has grown. The present material was collected over a period of three years. There is another question to which the material is large enough to furnish an answer: If cancer is more frequent in the family of cancer patients does the surplus of cancer cases appear without any regularity in the families of the patients, or is there an accumulation in certain families? Our material of 250 cancer cases has been divided into two categories. The first group contains all the cases of cancer, where two or more other cancer cases were found in the family. The second group contains all the other cases. In this latter group there was at most one other cancer case in the family in addition to the cancer case. The second diagram shows this. It is arranged in exactly the same manner as the first one. It consists of three parts. The first (I) and second (II) are the cases of comparison and the cancer cases. The third part (III) is the diagram of the cancer cases in which there were no other, or not more than one other cancer case in the family in addition to the cancer case. All the cancer cases with more than two other cancers in the family are crossed out. In this diagram it is evident that there is no difference between the last group and the cases of comparison. All the differences between cancer and non-cancer have disappeared. This shows that the group of cancer in general can be divided into two categories: One group where a distinct accumulation of cancer cases in the family was evident; and a second group of cancer cases where no more cancer appeared in the family than in the cases of non-cancer. Quantitatively the last group is much larger than the first (200:50). From this material we can draw the following conclusions:

1. In a series of families of cancer patients cancer is more frequent than in any other series of families.
2. The surplus of cancer in the family of cancer patients always accumulates in certain distinct families.
3. There is a large group of cancer patients in whose family cancer is absolutely not more frequent than agrees with the "normal" chance of dying of cancer.
4. Hereditary influences are only evident in a small category of cancer cases.
5. So far as can be judged from the material, there is no difference between the groups alluded to in 3 and 4 so far as the localization of the primary tumor is concerned.

## IS CANCER A SYSTEMIC DISEASE?

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WHEN the average medical man of today hears the word "cancer," his mind will likely react thereto with the picture of a tumor, or, if he should happen to be one of those who, in recent years, has come to recognize the advisability of attacking cancer therapeutically in the precancerous state, he may see in his mind's eye a chronic dermatosis, a fistula, a benign tumor, or the like.

There seem to be as yet, however, but few clinicians who are willing to concede that precancerous lesions and malignant tumors are, in all probability, symptoms of preceding, more deep-seated morbid conditions, and that not unlikely a cancer-patient's whole system is abnormal long before any sign becomes noticeable which is commonly called suspicious. Their hesitation to fall in with such notions is readily understandable.

The conception of cancer as a systemic disease seemingly reverts to antiquated ideas which have been denounced as heresies by generations of medical men. These students sought in the cell alone the hidden secret of the cancer problem and, more or less, disregarded possible influences of the humors. However, in the light of the results obtained by the improved methods of investigation which we now command, this school appears to have been somewhat too radical in its condemnation of the systemic conception of cancer etiology and to have without proper justification declared obsolete the experience of the old-time keen-witted bedside physicians who diagnosed not from small specimens of excised tissue, but had always before them and examined the whole patient.

In this observance the writer believes we shall have to follow the example of the ancient general practitioners, if otherwise we want to succeed in curing a cancer in such a way that it will stay cured.

This statement is, though, by no means intended to imply that we should return to their mode of treating cancer and should continue where they left off. On the contrary, while recognizing certain points of view of these old-fashioned practitioners as well taken, we also realize that the intervening progress of the medical art has not brought us back in a circle to where they stood, but has lifted us in a spiral above them. The lofty height of present-day scientific achievement permits us to look down hopefully upon their struggles with obstacles which in those more remote times were found insuperable.

From this point of vantage a position appears now no longer tenable which regards a malignant tumor as a thing *per se*, as having a pathology of its own, as subject to none of the laws which govern the other parts of the body of its



host, and as capable of exhibiting in its cells powers which exceed those possessed by normal tissue cells. These views would seem to be erroneous.

In contrast thereto, it appears more likely that all cells, and consequently all cancer cells as well, are the creatures of the conditions which surround them; that they must adapt themselves to these conditions, or else perish; that cancer cells have no energy of their own; that the energy they seem to possess is imparted to them by the vis-à-tergo exerted through the growing cell multiplication and the demand for space of the daughter cells, and that therefore tumors of every description are not active, but passive growths. That is to say, they do not grow like a green leaf through inside forces, but rather like a heap of dry leaves through outside forces without any contribution to the growth on the part of the heap.

The views referred to as erroneous regard the tumor as the primary phenomenon and know systemic involvement only after the malignancy has become generalized. On the other hand, the here advocated view starts with systemic disturbances as the primary disease, on the basis of which malignancy sets in as a secondary development.

For those sharing the first-mentioned views, cancer is a cell problem; for those supporting the standpoint mentioned in the second place, cancer becomes primarily a problem of the physico-chemical condition of the humors of the body.

As a cell problem, the explanation of cancerous phenomena has admittedly run up against difficulties which leave these phenomena in darkness. As a physico-chemical proposition, the cancer problem finds thrown open for the overcoming of these difficulties formerly unavailable avenues of explanation which seem to lead to the light.

Under this latter conception the problem becomes a complex composed of "a constitutional disease cancer," conceived of as grounded in certain systemic disturbances; and secondarily thereto, of "a new growth cancer," as a symptom of the presence of the constitutional disease.

This conception brings forward a number of questions, which are: first, what is it that disturbs the normal constitutional balance of certain individuals and originates in their system conditions which seem to predispose them to cancer? Second, what is it that in some of these presumably cancer-susceptible individuals causes the onset of developments of potentially cancerous character? Third, what is it that, once these developments have been started, causes their continuance and turns potentially cancerous new growths into malignant tumors?

As stated and supported in previous publications,<sup>1</sup> the answer to the first question, as to the original systemic involvement, is believed to be an inherited or acquired imbalance of the sympathetic and para-sympathetic (vagus) nervous systems which induce a disturbance of the endocrine gland and serum electrolyte balance, and, in addition thereto, the reflex action of this latter imbalance to further increase the nervous imbalance, a vicious circle. This vicious circle might well be considered to be a "systemic chronic irritation."

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The existence of the vicious circle is diagnosable as vagotonia. Individuals exhibiting this symptom, which, by the way, is not specific for cancer, we believe to become gradually predisposed to cancer, as will be shown by taking up the second question.

The answer to the second question, as to what on the basis of the foregoing primary disturbances causes developments of potentially cancerous character, is based on the gradual increase of the degree of alkalosis of the tissue fluids through the intensification of the vicious circle. Weakness of the nervus sympathicus has also been shown in the previously mentioned publications to disturb by way of the parathyroid glands the calcium metabolism and to produce a deficiency of calcium ions in the serum. In this way the normal calcium-potassium ratio in the serum would seem to be thrown out of balance in favor of potassium, whereby the water economy of the patient's whole system becomes abnormal.

Inasmuch as potassium goes with cell swelling through imbibition, and calcium goes with cell shrinkage through desiccation, calcium deficiency, *i.e.*, relative potassium excess in the serum, is believed to result, by imbibition, in a hydropic condition of the cells of the entire body of an individual affected with a primary nervous imbalance.

As a consequence of the abnormally increased water content of the cells, there are found here, in addition to vagotonia, an impaired healing capacity of the tissue and sometimes a certain unnaturally florid appearance of the individual. As a result of the impaired healing capacity acute lesions leave behind in cancer-susceptible individuals various states of local chronic irritation. These states are of potentially cancerous character in such individuals because they are apt to induce cell proliferation if left untreated and permitted to increase in severity through the combined action of the prevailing disturbances. It may not be out of place to repeat our belief that they can so increase only on basis of the before-mentioned systemic chronic irritation and that without this latter disturbance a local chronic irritation may exist ever so long and not become cancerous.

In this assumption the answer is found to the third question, as to what causes the progress from potential to actual malignancy. As stated, it is based on the complex effect of the combined action of the systemic and local chronic irritation.

The effect of the local chronic irritation is cell death in the irritated tissue. In the streaming tissue fluids the dead cells undergo necrobiosis. Their detritus is washed away and absorbed. The detritus consists of cell lipoids and of the decomposition products of the cell protein, *viz.*, amino-acids and their derivatives. These protein products we have called "necrones," an abbreviation of necrohormones.

Necrones have been shown, also in the before-mentioned publications, to enforce the division of cells exposed to their influence. The divisions follow one another the more rapidly the stronger the necrone influence. It is assumed that the necrones go into solution with the cell lipoids and that the influence

of varying degrees of the concentration of this solution underlies all cell performances. A degree of concentration within the limit of the physiological tolerance of the cells for necrones is believed to cause cell function and the hypertrophy of resting cells, reversible by cell atrophy. A degree of concentration exceeding this limit is believed to enforce the onset of cell proliferation, reversible only by cell death. In the point of change from cell rest to cell motility we place the beginning of the precancerous state.

Inasmuch as this change requires a degree of concentration of the necrone solution which exceeds that physiologically attainable, the question arises as to how in the streaming tissue fluids it can materialize. Of course, it cannot. In order to materialize it needs stagnation. Where do we find stagnation?

Here recourse had to be taken to a working hypothesis. It is based on the well-known fact that cells are of varying resistance to chronic irritation. It has, therefore, been assumed in the previously mentioned publications that of the locally irritated cells some die, while others undergo merely an impairment of their permeability. A group of microscopic size of thus damaged cells may be called a focus within which, relative to the velocity of the streaming tissue fluids outside the group, more or less stagnation prevails, the degree of stagnation and therewith the degree of concentration of the necrone solution depending on the degree of impermeability of the cells forming the wall of the focus, *i.e.*, on the severity of the local chronic irritation.

We now have that which will force cells to divide: the concentrated necrone solution. The question remains to be answered, why do the cells continue to divide? The focus furnishes the explanation. Inasmuch as it furnishes the stagnation within which the necrone solution can form and become concentrated, it would seem also to protect the concentrated solution against dilution. The daughter cells of the cells that had their division enforced by the concentrated solution, on coming into existence, therefore find themselves exposed to the same influence that had enforced the division of their mother cells, so that they on their part are now forced to divide, as are also other generations of daughter cells after them as long as the local chronic irritation keeps up its slow increase in severity. When it stops doing this, the proliferative process will be arrested; when it decreases, there probably will be recession of the forming tumor; on its renewed exacerbation, the process will resume its progression.

If we now do as did the bedside practitioners of old and examine the whole patient, what do we find? We recall that we are dealing with a complex of active disturbances, the combination of the local chronic irritation and the systemic chronic irritation, the primary vicious circle. When we now make exact measurements of the serum reaction, they reveal that both disturbances have been gradually getting worse. The originally discovered pre-disposing low-grade alkalosis of the serum was of a so-called premetastatic degree, that is to say, cells newly formed at the focus and carried away in the lymph stream, lost therein their viability and underwent necrobiosis. Their

detritus was absorbed and these cells disappeared completely. On reëxamination of the patient we now find a change to have taken place in the character of the tissue fluids. Their alkalosis has attained a degree in which disseminated malignant cells retain their viability. The serum has become metastatic and the vagrant viable cancer cells are apt to give rise to metastases.

Exact pH measurements have revealed the fact, as shown by the literature, that malignancy is always associated with a high degree of alkalosis, and it has also been shown that the alkalosis precedes the malignancy. There can be alkalosis without malignancy; but it would seem that there can be no malignancy without alkalosis. The more virulent the malignancy, the stronger must be the alkalosis which sustains it.

On examining our patient we find then that the combined effect of the systemic and the local chronic irritations has brought on a stage of the disease where, in consequence of the wide dissemination of viable cancer cells and the presence of metastases, the case would ordinarily be pronounced inoperable. But is there really nothing that can be done for such a case?

From the physico-chemical standpoint the answer appears obvious. If alkalosis is the *sine qua non* of tumor growth and tumor malignancy, why should not acidosis enforce the regression of the same? And so it seems to do, indeed. Close analysis of so-called miraculous cures, which hitherto had been left unexplained, has yielded this writer<sup>2</sup> the impression that acidosis produced in various ways, was the underlying cause of cure in all of them.

However, there are differences in degree clearly discernible. If the acidosis was merely relative, that is to say, if the alkalosis in which the malignant tumor flourished was reduced only to a lower level of alkalosis, there seemed to be temporary betterment and no cure. If clinical acidosis was produced, that is to say, acidosis below the normal blood reaction of the patient *i.e.*, below pH 7.39 to pH 7.33, in one instance pH 7.28 having been attained, there seemed to be a definite cure and the patient stayed cured for a number of years. Tumor and metastases had disappeared and the system had been cleansed of disseminated cancer cells, so that there was no more danger of recurrence of the former condition.

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# THE INTERRELATION BETWEEN HEREDITARY PREDISPOSITION AND EXTERNAL FACTORS IN THE CAUSATION OF CANCER

I. NEOPLASMS IN MICE AT THE SITE OF GROSS TRAUMAS  
Studies in the Incidence and Inheritability of Spontaneous  
Tumors in Mice. 30th Report

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Two urgent lines of research in cancer confront us. First, studies in the etiology of cancers to the end that eventually, if it be possible, we may find methods of eliminating these diseases completely. This includes studies in hereditary predisposition which provide the susceptible individuals. Second, studies in the external provocative causes of cancers, in order that we may learn to prevent the development of cancers in persons susceptible by heredity. For these external irritations, which are not cancer-producing under ordinary conditions, when they are applied to a cancer-susceptible subject, seem to be an important factor in the occurrence of cancer. This fact gives us one of our greatest hopes for preventing cancer, until such time as we find a method of eliminating the disease, or in case we never find such a method.

The goal of the studies in cancer carried on in this laboratory has always been the collection of data concerning spontaneous cancers, which might aid in the prevention of cancers, rather than to seek for cures. It is for this reason that during the past twenty years I have put out some twenty-nine reports concerned chiefly with the etiology of cancer, the relation of hereditary predisposition to the occurrence of cancers, and the way these hereditary predispositions behave in cancer incidence, as this must be the fundamental background for future studies and for preventive methods.

As early as the second report of this series, however, in 1914, I recognized the importance of the external factor in cancer occurrence.<sup>1</sup> Again in the third report<sup>2</sup> I described at some length the relation of external provocative factors in the occurrence of cancers in mice with hereditary predisposition thereto. I stated as follows: "Tumors of the mouth and jaw are rare in mice. But there are just *two causes of chronic disorders in the oral region of mice, viz., the overgrowth and consequent pressure of an irregularly placed tooth, or a wound caused by fighting or by being hurt in the cage.*" I mentioned at that time female 7,618 (the subject of protocol 13 in this series) with her neoplastic growths at the site of a wound occasioned by an accidental blow from a cage door.

In later publications also, more or less casual reference has been made to the external factor in cancer causation. This matter was also discussed at length in the twenty-sixth report.<sup>3</sup> But the hereditary predisposition, as

the soil for the development of cancer, has always been particularly stressed. It is a somewhat difficult matter to collect a sufficient amount of evidence to be conclusive in showing the relation of external factors in spontaneous cancer causation. Hence I have delayed the report of this part of my studies until this time.

It is my intention now to put out a series of papers, of which this is the first, which will deal with data furnished in my laboratory, bearing upon the relation of external agents to the occasioning of spontaneous cancers. This first paper will deal only with the relation which external gross traumas seem to bear to the occasioning of cancers in susceptible subjects. It will include only those cases arising in my first 14,000 necropsies, in order that these may be handled in some detail, while still keeping the paper within the allotted length. Similar cases arising in the rest of the 92,000 necropsies performed to date must await later publications.

In the first 14,000 of these necropsies there occurred 1,301 indisputable neoplastic growths. Of these, fifty-one arose under observation at the sites of recorded gross traumas. Many more of these neoplasms may have been at the site of gross traumas, but the traumas were not observed at the time of their occurrence and by the time the growth was found the evidence of trauma was lost in the growth.

These fifty-one neoplasms were distributed as follows; twenty-four were in males and twenty-seven in females. This small predominance of females is unimportant, as the wounds of males are frequently received in fighting, and generally are so severe as to be fatal almost immediately, so that there is no opportunity for reparative processes.

These neoplasms occurred at practically every external site where wounds are possible. The locations were as follows:

- 5 in the testicle.
- 4 in the subcutaneous tissues of thigh and inguinal region.
- 5 in the mammary gland.
- 6 in the knee.
- 4 in the face.
- 7 in the subcutaneous tissues of the back.
- 1 in the outer aspect of the chest wall.
- 2 in the abdominal body wall at the base of the ribs.
- 2 in the mouth.
- 1 at the base of the throat.
- 3 in the foreleg and foot.
- 2 in the pelvis near a broken hip.
- 2 in the hip bone.
- 3 in the hind leg. (One of these mice showed liver and skull metastases, one showed pelvic extensions and the third had also thymus lymphosarcoma, retroperitoneal, pelvic and pancreatic lymphosarcomas.)
- 2 in the retroperitoneal tissues (with pancreatic extensions).

- 1 in the prepuce.
- 2 in the tail. (Both of these mice had leukemia also.)
- 1 in the penis.
- 1 in the subcutaneous tissues of the neck. (This mouse had also pseudoleukemia.)
- 1 generalized throughout the subcutaneous tissues.
- 1 at the base of the ear.

In some cases wounds followed by neoplasms occurred in more than one site in the same mouse.

In addition to these mice wounded in external sites, there were also three cases of neoplasms in the liver which developed in male mice, each of which had been wounded and deeply bruised subcutaneously, immediately over the locations of the liver tumors. I am including their protocols as the *juxtaposition of the subcutaneous wounds and the liver neoplasms suggests that the liver also may have been injured at the same time as the subcutaneous tissues. These cases may therefore be of interest.*

### TYPICAL PROTOCOLS

1.—♂ 585 was a member of strain 90, a highly tumorous strain. He was the son of female 31 with a sarcoma of the thyroid and a sarcoma of the thymus; and of male 167 that died of panophthalmitis. He was the grandson of female 3 (classic in these studies) that died of a mixed sarcoma-carcinoma of the mammary gland, a malignant adenoma of the liver and sarcoma metastases in the kidney. His grandfather, the brother of female 3, was male 30 that died of chronic interstitial nephritis and general amyloidosis without cancer.

This male 585 when about nine months of age, received minor injuries to the genitals in fighting. He was isolated for observation and while under observation developed a spindle-cell sarcoma in the left testicle upon the site of wounds. The immediate causes of his death, however, were myocarditis and œdema of the lungs.

The tendency to sarcoma in this line of the descent is notable, there being here three straight generations of sarcoma. The grandmother, female 3, with her mixed sarcoma-carcinoma of the mammary gland and sarcoma secondaries in the kidney, evidently in this line transmitted pure sarcoma. I consider this transmission of pure sarcoma (as well as pure carcinoma in some cases and mixed tumors in other cases) by female 3, as the best possible evidence for the very certain existence of these mixed tumors which have been under much dispute.

Male 585 is referred to on page 217 of the twelfth report<sup>4</sup> of this series which deals with the testicular tumors in the first 19,000 necropsies of this work.

2.—♂ 596 was also a member of strain 90, having female 3 and male 30 for his grandparents also. His mother, 73, died of primary carcinoma of the lung, and his father, 752, died without cancer, of an unknown infection involving liver necrosis. He was the cousin of the foregoing male 585. He was isolated in "hospital" for observation after receiving multiple small bites on the genitals and upon the body. While under observation he developed a subcutaneous mass at the site of one of these wounds. The penis had been rather severely injured. The healing caused closure of the urethra,

urinary retention and uræmia, which were the immediate causes of death. The subcutaneous nodule at the site of one of the wounds proved to be an adenoma. Adenomas and carcinomas occurred in the ancestry of this mouse.

3.—♀ 890 was a member of strain 264 which carried a number of tumorous individuals. The early generations of the strain have been charted and described on page 285 of the second report referred to.<sup>1</sup> It had at that time produced about 16 per cent. of neoplasms. The father and mother of male 890 both died before autopsies were begun. It is impossible to know whether they had tumors, but they had no external growths. Male 890 was badly bitten in fighting. He was isolated and under observation three weeks. He died of intrathoracic hæmorrhage, probably as a late result of his wounds. At autopsy a subcutaneous spindle-cell sarcoma was found on the left thigh at the site of a wound. Sarcomas, as well as adenomas and carcinomas lay behind this mouse.

4.—♀ 1376 was a member of strain 177 which produced many neoplasms. The strain has not yet been published. She was born on December 30, 1910, and died May 10, 1912. Her mother 260 died in labor without cancer. Her father was male 596 with the subcutaneous sarcoma described above. She was wounded in the inguinal region by her mate, male 1672, and was then isolated for observation. On the site of the inguinal wound there arose a small neoplasm which proved to be an adenoma of the mammary gland. Her death was caused by an abscess in the left kidney which also was sequel to her wounds. Adenomas and carcinomas lay behind this mouse.

5.—♂ 1470 was the parent of branch A of strain 53 which was charted on page 123 in the eighteenth report of this series.<sup>5</sup> His mother was female 3 already referred to in these protocols, and his father was male 40 that died of uncertain causes, the only abnormality found being a small cyst in the region of the urinary bladder.

This male 1470 was bitten about the genitals and on the belly. He was isolated for observation. He died about seven weeks later at the age of one year, five months, twelve days, showing at autopsy a hernia of the right seminal vesicle with urinary retention; right hydronephrosis; hypertrophy of the heart with pericarditis; œdema of the lungs and bilateral hydrothorax. He had also a malignant adenoma of the liver like his mother, female 3. This adenoma of the liver was in the vicinity of the belly wounds and suggests injury to the liver received at that time.

Male 1470 was mated with his sister, female 13, that had a mixed mammary gland sarcoma-carcinoma which closely resembled that of her mother, female 3. She had also pure sarcoma metastases in the lungs and mesentery. From this mating of two neoplastic mice (female 13 by male 1470) branch A of strain 53, a 100 per cent. cancer strain was derived. One hundred per cent. of the mice of this family that lived into cancer age (six months or over) had neoplasms.

6.—♂ 1506 was a member of strain 34, a tumorous strain made by the crossing of two tumor strains, both of which were in their origins hybrid derivatives of classic strain 90, and both of which reach back in their ancestry to female 3.

The mother of male 1506 was female 721 of the first generation of strain 21, that died of carcinoma of the mammary gland with metastases in the lungs. She was the granddaughter of female 3. She is charted in the fifth and seventh reports of this series.<sup>6, 7</sup>

His father was male 2549, a member of the first generation of strain 41 (also derived from strain 90), and grandson of female 3. He died of intestinal infection without cancer.

Male 1506 was bitten about the genitals and belly. He was isolated for observation after being bitten the second time so badly as to cause closure of the urethra followed by acute nephritis and uræmia. At autopsy he was found also to have a malignant adenoma of the liver. Mated with his sister 3673 with a carcinoma of the mammary gland, he produced the 100 per cent. cancer branch of strain 34. One hundred per cent. of those that lived to cancer age had cancer.



7.—♂ 1717 was the son of adenomatous female 1376 described in protocol 4, and male 1672 that showed at autopsy interstitial nephritis and some necrosis of the liver tissue but no neoplasm. He was therefore the grandson of tumorous male 596 (protocol 2) and hence derived from original female 3. Like the two foregoing cases, males 1470 and 1506, he was bitten about the genitals and the belly, and was isolated under observation. At autopsy about two months later, he disclosed an adenoma of the liver adjacent to the subcutaneous wound.

These three cases, 1470, 1506, 1717, have been included here because all three were derived from the same original ancestry, namely, female 3, with a malignant adenoma of the liver; all three were bitten about the genitals and upon the belly; all three survived to make reparative processes about the external wounds; and all three disclosed at autopsy an adenoma of the liver immediately adjacent to the belly wounds.

8.—♂ 3117 was a member of branch IV of strain 146 frequently charted in this series of studies. See chart opposite page 164 of the third report<sup>2</sup> for this branch of the strain, and page 178 of the third report for the ancestry of strain 450, of which 3117 was a member. He was the son of double cancerous parentage; his mother 1805 had carcinoma of the mammary gland metastasizing in the lungs: his father 3553 had leukemia. His grandmother 529 had a mixed sarcoma-carcinoma of the mammary gland metastasizing in the lungs. His niece 5229 is described in the ninth protocol of this paper.

Male 3117 was picked up on the field of battle bitten about the genitals and on the mammary gland tissue of the left side near the axilla. He was kept under observation for about two months, during which time he developed a spindle-cell sarcoma involving both testicles, and a second spindle-cell sarcoma of the left axillary mammary gland. Six of his brothers also engaged in the fight, but 3117 was the champion, and the others died almost immediately of their wounds without reparative processes.<sup>8</sup>

9.—♀ 5229 was a member of the fifth generation of branch IV of highly cancerous strain 146. Strain 146 frequently has been charted and described in this series of studies. See pages 164-171 of the third report referred to<sup>2</sup> and<sup>9</sup> pages 233-236 of the ninth report.

5229 was the daughter of cancerous female 3768 with four primary carcinomas of the mammary gland metastasizing in the lungs, and of hybrid carrier male 4933 that died of uncertain causes without cancer. She was the offspring of seven successive generations of cancer. Two of these generations had double cancerous parentage. Strain 146 was a hybrid derivative of 100 per cent. cancerous strain 139, which was also charted in both of the above reports. See page 164 of the third report and page 215 of the ninth report.

5229, at about eight months of age, was discovered on June 18, 1913, to have an early neoplasm in the left inguinal mammary gland. At this time her left hind knee had been hurt by being caught in the cage. She was placed under observation on this date and while under observation developed a hard growth on the knee at the site of the injury. Meanwhile her mammary gland cancer also progressed. She died August 3, 1913, at which time she was found to have a large alveolar carcinoma of the mammary gland and a fibrosarcoma of the knee.

10.—♂ 5695 was a member of the second generation of branch I, strain 150, frequently charted and described in these studies (notably in the twenty-first report<sup>10</sup> and on pages 91 and 93 of the twenty-seventh report.<sup>8</sup> He was the son of two hybrid carriers of cancer susceptibility, female 6488 and male 5426, both of which died of uncertain causes without cancer. He was the grandson of cancerous female 3383 with two mixed sarcoma-carcinomas of the mammary gland, and was a member of the sixth generation from male 274, parent of strain 145, with primary carcinoma of the lung.

Male 5695 was picked up on the field of battle July 8, 1913, badly bitten in sub-

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cutaneous tissues near the right shoulder. He was under observation from this date, and on September 15, 1913, showed a neoplastic growth at the site of the wound, which was then fairly covered with scar tissue. This growth extended dorsally to the mid-line, ventrally to the axilla and chest wall, and by the time the mouse came to autopsy measured forty by thirty-five by thirty millimetres. The growth proved to be a small spindle-cell sarcoma. Sarcomas, carcinomas and mixed tumors lay behind this mouse.

11.—♂ 6504 was a second generation member of strain 343 which is charted with its parentage in the third report on pages 174-176 and on page 291 of the ninth report of this series. He was the son of female 6357 with three carcinomas of the mammary gland metastasizing in the lungs, and of male 5850 that died of wounds without cancer. His immediate ancestry showed six consecutive generations of cancer, two of which had double cancerous parentage.

On December 19, 1913, he was found to have been bitten on both sides of the face and on the genitals. He was kept under observation until February 6, 1914, the date of his death. During this time he developed on both sides of the face at the sites of his injuries large fibrosarcomas which deeply infiltrated muscle, gland tissue and bone. He showed at autopsy also two papillary adenomas of the right upper and the left lower lobes of the lung. Sarcomas, carcinomas and adenomas lay behind this mouse.

12.—♀ 6629 was the daughter and the granddaughter of mice without cancer but they were hybrid carriers of the cancer tendency. Her maternal great-grandmother was female 529 with a mixed sarcoma-carcinoma of the mammary gland with metastases in the lungs. Female 6629 was bitten on both sides of the face by her mate, male 7470. While under observation she developed on the sites of these injuries bilateral spindle-cell sarcomas, and died in giving birth to her last litter of young (a litter of seven) on February 22, 1914, six weeks after receiving the wounds.

She was a member of branch IV, strain 164, which at the time of charting had shown cancer in about 24 per cent. of its members that lived six months or over. Charts showing this mouse and her ancestry have appeared in several reports of this series. For example page 500 of the fifth report.<sup>6</sup>

13.—♀ 7468 was the sister of female 6629 of the twelfth protocol. She was bitten on the back by her mate. At the site of this injury she developed a spindle-cell sarcoma which infiltrated through to the peritoneum. At autopsy her entire body was nearly bald, the wound on the back was covered with thick scar tissue and the sarcoma which distorted the whole body. The peritoneum proved to be extensively involved.

It is interesting to note in comparison with these two sisters, members of a highly tumorous strain, the reaction of many female members of non-cancerous strains, that have been wounded in the same way as females 6629 and 7468, without in any case the occurrence of a neoplasm.

14.—♀ 7618 was a member of 100-per cent. cancerous branch B of highly tumorous strain 84, frequently charted and described in this series of studies (especially on pages 115-122 of the eighteenth report).<sup>5</sup> She was the sister of female 8702 with carcinoma of the mammary gland and primary carcinoma of the lung, and of male 11777 that died of carcinoma of the lung with metastases in the chest wall and kidney. For lack of space she was not included in the chart on page 116, but her background of cancer susceptibility is there shown.

On May 28, 1914, the left angle of the mouth of 7618 was deeply slit by an accidental blow from a cage door, that cut the face halfway to the eye and down on the chin. This mouse was, on this date, placed under observation, and as reparative processes went on proliferation in this region was very soon apparent. The mouse died on June 22, 1914, at which time at the site of the deep cut there was a tumor measuring twelve by ten by five millimetres which proved to be a squamous-cell carcinoma, beneath which there was a spindle-cell sarcoma. The blow had cut not only the epithelium

but also the deeper-lying connective tissues. There was, apparently an attempt at regeneration in both tissues, which resulted in a squamous-cell carcinoma on top of a spindle-cell sarcoma.

15.—♂ 7983 was a member of 100 per cent. cancerous branch A of strain 73. His ancestry is charted on page 155 of the sixteenth report of this series.<sup>11</sup> He was badly bitten in two places on the left side, the two bites involving the abdominal wall at the base of the ribs and dorsal thereto. At the site of each of these two wounds there developed a spindle-cell sarcoma, about eight millimetres in diameter each, that metastasized in the diaphragm on the pleural side, in all lobes of the right lung and in the inferior mediastinum. This mouse is described in some detail in the eighth report of this series.<sup>12</sup>

16.—♀ 8077 was a member of the third generation of strain 343, charted in reports 3 and 9 of this series. She was the daughter of double cancerous parentage. Her mother, female 7039, died of a carcinoma of the mammary gland metastasizing in the lung, and her father was male 6504 (described in the eleventh protocol), that died of bilateral fibrosarcomas of the face at the sites of wounds. Behind female 8077, therefore, in her immediate ancestry, there lay seven consecutive generations showing cancer.

She herself was accidentally struck on the mouth by a cage door in the hands of a careless diener. At the site of this wound, while under observation, she developed scar tissue, beneath and surrounding which was a spindle-cell sarcoma. At autopsy she showed leukemia which was verified by microscopic examination and blood count, and she had also lymphoid hyperplasia, and cystic degeneration of the mammary gland.

17.—♀ 8212 was a member of strain 367, an offshoot of strain 304 charted opposite page 172 in report 3<sup>2</sup> of this series and on page 164 of the sixteenth report of this series.<sup>1</sup> She was the offspring of three generations of double cancerous parentage and a member of a 100-per cent. cancerous family. Her great-grandmother 4514 died of a carcinoma of the lung (first diagnosed as adenoma and later as carcinoma). Her great-grandfather 5162 had tremendous subcutaneous lymphosarcoma extending from the neck to the inguinal region. Her grandmother 6685 had two spindle-cell sarcomas of the mammary gland. These tumors were first erroneously diagnosed as carcinomas but later, upon further study, they proved to be spindle-cell sarcomas. Her grandfather 7280 had a carcinoma of the lung and an adenoma of the lung. Her mother 7862 had carcinoma of the mammary gland and her father 8345 had squamous-cell carcinoma on the basis of a prolapsed rectum. Her four sisters, 7944, 7796, 8011 and 8960, all had carcinoma of the mammary gland. Her brother and mate 9944 had carcinoma of the lung and adenoma of the lung. The background here of cancer is thus very extensive.

Female 8212 was found with a subcutaneous wound at the base of the chest. While under observation she developed at this site a squamous-cell carcinoma in the midst of scar tissue over the wound.

18.—♂ 8579 was a member of cancerous strain 228 not yet charted in these reports. His mother 8125 had two carcinomas of the mammary gland, his father 6706 died of wounds, showing only advanced senile atrophy and little other change.

Strain 228 was a hybrid strain derived by crossing cancerous strain 47 with cancerous strain 146. The parents of strain 228 were female 3348 with two primary carcinomas of the mammary gland, and male 2805 that died of a liver abscess without cancer.

Male 8579 was bitten in the left inguinal region. At this point while the mouse was under observation, there arose a squamous-cell carcinoma with marked infiltration of the muscle. Such wounds in males of non-cancerous strains have never been followed by neoplastic growths of any kind during these studies.

19.—♂ 8986 was a member of cancerous strain 462 derived on the paternal side from strain 367, which in turn was derived from strain 304. As both of these latter strains were highly cancerous, there was a long line of cancerous ancestry behind male

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8986. His grandmother 8740 had squamous-cell carcinoma at the base of the ear. His grandfather 7730 died with senile atrophy, with few other gross changes, and without tumors. His mother 8836 had a fibrosarcoma of the abdominal wall adherent to the liver, probably at the site of an injury. But as this point is not perfectly certain, she is not included in this list of mice whose neoplasms certainly arose at the site of gross trauma. His father 8338 died of uncertain causes without cancer.

Male 8986 was found to have an injury on each knee. While he was under observation there arose a two-millimetre hard mass on each knee. These masses proved to be osteoid sarcomas.

20.—♀ 9128 came of a highly tumorous strain 16. She received two wounds on the back and upon the neck from her mate. At the site of these wounds on the back there arose scar tissue with a spindle-cell sarcoma beneath the scar tissue. At the site of the neck wound there was an abscess invading a second spindle-cell sarcoma. She had leukemia also.

21.—Male 9161 was a member of tumorous strain 135. He was accidentally cut across the right foreleg nearly to the bone, with the edge of a cage door. Two weeks later, on December 21, 1914, sarcomatous tissue was observed at the site of the wound. The mouse died January 9, 1915, with a spindle-cell sarcoma which involved the entire foreleg and the entire foot except the extreme tips of the toes.

22.—♂ 9293 was a third generation member of highly cancerous strain 338 repeatedly reported in these studies. He will be found on the chart of this strain opposite page 516 in the seventh report.<sup>7</sup> In that chart he was stated as dying of wounds. He had been badly bitten about the genitals and the left hind leg. Upon the site of the wound on the left hind knee there was a hard nodule ten by eight by six millimetres. This nodule was not caught by the technician in making the first sections, and it was not until after the publication of this report that the nodule was decalcified and found to be osteoid sarcoma. This mouse had an immediate ancestry behind him of eight consecutive generations of cancer. His mother 10442 died of general sepsis from tapeworm, without cancer, and his father 11319 of a carcinoma of the lung. The neoplastic sequence in parents and grandparents of each generation behind 9293 was as follows:

1st generation: female with sarcoma-carcinoma of the mammary gland, malignant adenoma of the liver, and sarcoma secondaries in the kidney.

2nd generation: female with carcinoma of the mammary gland; and female with carcinoma of the lung.

3rd generation: female with carcinoma of the mammary gland and metastases in the lung.

4th generation: female with malignant adenoma of the liver; and female with malignant adenoma of the liver and adenoma of the mammary gland.

5th generation: male with carcinoma of the lung.

6th generation: female with carcinoma of the mammary gland, carcinoma of the pelvis and metastases in the lungs; and male with an adenoma of the lung.

7th generation: female with two carcinomas of the mammary gland; and male with adenoma of the liver.

8th generation: male with carcinoma of the lung.

9th generation: male 9293 with osteosarcomas at the sites of knee wounds.

23.—♀ 9350 of the same strain 338, also had a nodule on the knee at the site of an injury. This nodule also proved to be osteosarcoma. She died of hæmorrhage in the liver from tapeworm. She was the aunt of the foregoing male 9293 and appears on the same chart. As both of these nodules had to be decalcified, the final report on them had not been given when the chart was first published.

24.—♂ 9392 was a member of a 100-per cent. cancerous branch of strain, 186, published on page 501 of the fifth report of this series.<sup>8</sup> His mother 2849 had desmoid tumor of the back and sides, as had also his father 3053, his sister 10054, his brother

10079, his son 10924 and his niece 12275. This was a small family, every member of which beginning with 2849 had this particular type of neoplasm on the back and sides, and no other type of neoplasm whatever. Male 9392 was found with wounds on the back and sides and was placed under observation. In this family this type of neoplasm ran a certain course. First the back and sides became completely hairless, then the skin and subcutaneous tissues seemed to be thickening so that the mouse gradually became almost unable to move. At autopsy the tumors all were of the same desmoid type. This is particularly notable as there have been very few desmoid neoplasms in my stock outside of this small family. In the case of male 9392 the tumor quite evidently arose at the site of wounds. If any superficial wounds preceded the tumors in other members of the immediate family they were not found in time to be certain that they preceded the tumor growth.

25.—♀ 9446 was a member of strain 449. She came of two generations of cancerous individuals. Her grandmother 6062 died of pulmonary infection without cancer. Her grandfather 5079 had spindle-cell sarcoma of the mammary gland. Her mother 7594 had two carcinomas of the mammary gland and lungs riddled with metastases. Her father 7472 died of uncertain causes without tumor, few changes being evident at autopsy.

9446 was found, on December 28, 1914, to have a small mass in the left flank. She also had slight wounds (from bites) in the left axilla and the left anterior mammary gland. She was placed under observation and during the period between December 28, 1914, and February 17, 1915, the date of her death, developed a second carcinoma (in the axilla) and a third carcinoma (in the anterior mammary gland) at the sites of the bites.

26.—♀ 9513 was a member of tumorous strain 135. She was the daughter of male 9161 of the twenty-first protocol herein, that died of spindle sarcoma involving the entire foreleg and foot to the tips of the toes, and which arose at the site of a deep cut. Her mother 8021 died when only three months old of uncertain causes without cancer. Her grandmother 4339 died of two carcinomas of the mammary gland with secondaries in the lung and mediastinum. She had also a primary adenoma of the lung. Her great-grandfather 1630 had carcinoma of the lung with metastases in the lungs.

9513 was found on January 5, 1915, with a broken left hip, with no recognizable tumor at the site of the injury. She was isolated for observation. She died February 24, 1915. I quote from the autopsy findings: "Within the pelvis on the left side is a tumor mass twenty by eighteen by eighteen millimetres which seems to have arisen at the point of the fractured hip from pressure of the broken bone. The tumor extends over the kidney but lies dorsal from the left horn of the uterus and involves neither organ." This mass proved to be an osteoid sarcoma.

27.—♀ 9554 was a member of strain 145 charted in the twenty-first report of this series. She arose three generations later than the last generation shown in the chart, but her ancestral background is therein shown. She was a member of a highly tumorous branch of her strain. Her grandmother was 3383, with two mixed sarcoma-carcinomas of the mammary gland.

9554 was found with a broken femur at the left hip on January 25, 1915. A small subcutaneous abscess on the hip had been noted November 12, 1914. This abscess cleared up, but it may have caused infection in the hip occasioning the later fracture. The mouse died March 1, 1915, at which time there was an osteosarcoma twenty by sixteen by sixteen millimetres arising at the fractured hip. She had been dragging this hind leg since the fracture noted on January 25. The sarcoma spread into the pelvis and retroperitoneal tissues, involving the peritoneum and the body wall. The liver was riddled with secondary nodules. The spleen contained a small secondary nodule in its upper surface and all lobes of the lungs were riddled with metastases. 9554 is described in the eighth report of this series, page 17.<sup>22</sup>

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At the sites of wounds described in the foregoing protocols, there arose neoplastic growths as follows:

|                               |                  |
|-------------------------------|------------------|
| 12 spindle-cell sarcomas      | 2 adenomas       |
| 4 carcinomas                  | 1 desmoid tumor  |
| 5 osteo- and osteoid sarcomas | 3 fibrosarcomas. |

Forty-two per cent. of these cases thus were spindle-cell sarcomas, while each of the other neoplastic types occurred in small numbers. I have also included in this series of protocols, three cases of liver adenoma in male mice. These adenomas were immediately adjacent to deep abdominal wounds, and this fact seems to suggest that the liver was injured as well as the subcutaneous tissues when the wounds were received. There are notable cases where more than one member of the same family developed the same type of neoplasm at the sites of similar wounds, and there is, behind every case, the significant neoplastic ancestry, particularly classic female 3 with her mixed sarcoma-carcinoma of the mammary gland, malignant adenoma of the liver, and sarcoma secondaries in the kidney, who was the original progenitor of many highly cancerous strains.

There have been in my laboratory, stocks which have never to date produced a neoplasm of any kind, either in their original strains or in their hybrid derivatives. Such strains I have called "non-cancerous" strains. Within these non-cancerous strains identical gross traumas have occurred quite as frequently as in the cancerous strains, without in any case the arising of neoplasms.

I have given herein only the facts concerning a very few of the cases arising in the first 14,000 necropsies of my stocks, where hereditary predispositions and recorded external gross traumas were both present, and seem to have been interrelated in occasioning the occurrence of cancers. Only the limit set upon the length of this paper prevents the presentation of many more such cases. The conclusion seems unavoidable that in the cases herein described hereditary predispositions and external gross traumas were the interrelated causes of the occurrence of cancers.

It is my intention, as quickly as possible, to put on record all such occurrences in my stocks, as well as the occurrences of neoplasms following other apparently cancer-provocative external factors. I shall not, at this time, speculate on this apparent interrelation between hereditary predispositions and gross traumas in the causation of cancers, nor upon its application. Only the first group of data is herein presented.

# CANCER AND SMOKING HABITS

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POSSIBLY no phase of the highly complex cancer problem offers better opportunity for practical results than the general admitted correlation of excessive smoking habits to cancer of the buccal cavity, pharynx, larynx and œsophagus. Medical literature makes record of some outstanding illustrations from Emperor Frederick II of Germany to General Grant, who are known to have died of cancer of the throat attributed to excessive habits of smoking. Yet the question in general has not by any means been so fully elucidated by means of ascertainable and conclusive data as the urgency of the subject would suggest. In fact, I know of no really comprehensive statement of the whole question presenting modern facts suggested by the profound changes in smoking habits, including the wide extension of the practice of cigarette smoking to a considerable proportion of women.

It would not, of course, be feasible for me on this occasion to survey even the major aspects of the problem. But a few preliminary observations are called for in explanation of the medical data to be discussed in some detail, representing as they do entirely new information secured as part of my San Francisco Cancer Survey, and of other sections and localities.

Smoking habits in their relation to disease occurrence cannot possibly be considered without regard to

1. The kind of tobacco smoked.
2. The daily average quantity smoked.
3. The daily habits of smoking.
4. The form or method of smoking.
5. Date of commencing to smoke.
6. The regularity or irregularity of the habit in individual cases.

I can touch only very briefly upon some of these points by way of explanation. The nicotine content of tobacco varies widely in the different varieties. According to a recent report of the Connecticut Experimental Station, the total nicotine content of ordinary unprocessed pipe tobacco varied in eleven samples from a maximum of 2.8 per cent. to a minimum of 1.25 per cent. The average content for all samples of standard brands was 2.04 per cent.

In ten samples of standard brands of cigars, the range in nicotine content was from 1.90 per cent. to 0.91 per cent., the average for all samples having been 1.51 per cent.

In forty-six samples of standard brands of cigarettes the range in nico-

tine content was from 3.34 per cent. to 0.43 per cent., the average for all samples being 1.77 per cent.

Hence it is shown that in the order of average nicotine content, cigars have the lowest average percentage, or 1.55 per cent., followed by cigarettes with an average of 1.77 per cent. and by pipe tobacco with an average percentage of 2.04 per cent. But these figures are of academic rather than of practical importance in that the actual quantity of tobacco smoked varies considerably as to whether the smoking is by means of pipe, or large-sized cigars, or from one to three packages of cigarettes a day. To ascertain the exact facts for a large number of individual smokers would, therefore, be quite a formidable undertaking.

Furthermore, daily habits of smoking differ enormously. Some persons (this applies to both men and women) smoke practically all day long, starting even before breakfast and ending just before going to sleep. Others smoke only after meals, and still others at regular intervals. Then again, some persons learned to smoke very early in life, say at ten or twelve years of age, while others acquired the habit late in life, when the possibility of injury must have been measurably less, particularly to the soft portion of the buccal cavity and the highly sensitive portion of the pharynx and larynx.

Nor can the profound changes in smoking habits on the part of the present generation be ignored. Cigarette smoking has very largely replaced the smoking of cigars, while the latter to a considerable extent have taken the place of the pipe. The use of the old-time clay pipe, in this country at least, has almost disappeared. In this connection I quote the following statement from the Commerce Year Book for 1929.

Cigarette production in registered factories passed the hundred billion mark for the first time in 1928, amounting to 105,927,000,000 in number, besides which 9,233,000,000 cigarettes for export were manufactured in bonded warehouses, making the total output 115,160,000,000. The average annual increase in production from 1920 to 1928 was about 7,300,000,000. The consumption of cigarettes in the United States in 1928 amounted to 102,765,000,000, an increase of 5.6 per cent. over 1927; the number per capita was 856 compared with 820.

As regards cigar production it is stated:

Cigar production during the last five years has shown little change, standing at a level somewhat lower than during the immediately preceding years or than before the World War. The output in 1928 was 6,874,000,000. The consumption of cigars in the United States, although not as great as before the cigarette became so popular, is larger than in any other country.

As regards the general effects of smoking on health, there is a variety of widely conflicting medical opinion. I may quote from a report by Dr. W. M. Johnson, which is rather favorable to the smoker, as pointed out by Dr. W. E. Evans, of Chicago, in an article on the subject. Doctor Johnson's conclusions are as follows:

1. Tobacco smoking apparently has no permanent effect on the blood pressure.
2. If it affects blood pressure at all, it temporarily reduces it.



3. It is doubtful whether tobacco plays a major part in causing angina pectoris.
4. The effect of tobacco smoking is chiefly local, exerted principally on the pharynx.
5. There is no foundation for the popular belief that smoking decreases the weight of an individual.

Nothing, in these observations, is said as to the possible correlation of smoking habits to cancer, which at the same time is one of the most striking phenomena of the practice.

The first question of importance for the present purpose is the extent to which smoking is practised in a normal population. There are some interesting statistics on this point in an article by Dr. Emil Bogan, of Cincinnati, contributed to the *Journal of the American Medical Association* of October 12, 1929. He gives returns for 630 men in an industrial population, of whom 282 were non-smokers, or 44.8 per cent.; 269 were light smokers, or 42.7 per cent.; and seventy-nine were heavy smokers, 12.5 per cent.

I have returns obtained by special investigators from living cancer patients in San Francisco, Buffalo, Boston, and some six or seven other cities representing a normal cancer population. Of the 1,416 male patients closely questioned 282 or 20.8 per cent. were non-smokers, 33.6 per cent. were moderate smokers, and 45.6 per cent. were heavy smokers. For cancer of the buccal cavity the respective percentages were as follows; non-smokers, 16.2 per cent., moderate smokers, 36.5 per cent., heavy smokers, 47.3 per cent. The percentages are based on 1,413 patients for whom smoking habits were ascertainable. In other words, for the entire group, 79.2 per cent. were smokers; while for cancer of the buccal cavity the percentage was 83.8 per cent. For cancer of the stomach it was 79.2 per cent. and for cancer of the intestines 66.3 per cent.

As regards particular smoking habits, I am afraid the returns are not entirely trustworthy, for it is seldom that a patient has only one smoking habit. In other words, a patient may almost always use a pipe but occasionally cigars also, while other smokers report the use of cigars and cigarettes in combination. Since there were 1,061 smokers, the number smoking pipes only was 349, but in addition there were 435 who admitted smoking pipes and cigars, a total of 78, or 73.9 per cent. For cancer of the buccal cavity only, this percentage was 81.1 per cent. Among heavy smokers, out of 607 patients returned as such, 232 smoked pipes only, while 223 additional smoked pipes and cigars, a total of 455, equivalent to a rate of 75 per cent. For cancer of the buccal cavity this proportion was 87.3 per cent. It is thus shown that the proportion of smokers is relatively largest among those who die from cancer of the buccal cavity and the same is true of pipe and cigars smokers, but the excess is not so marked as might have been expected. This, of course, is due to the fact that cancer of the buccal cavity represents a variety of tumor liabilities which have no connection with smoking habits, although it is highly suggestive that cancer of the buccal cavity is almost invariably much less common in the civilized populations among women than among men, but such cancers do occur.

I have subjected my statistics to a critical analysis by specific organs and parts. Selecting a few for the present purpose it is observed as follows: There were sixty patients with cancer of the cheek, of whom eighteen or 30 per cent. were reported as heavy smokers. There were thirty-eight patients with cancer of the jaw, of whom seventeen or 45 per cent. were heavy smokers. There were 120 patients with cancer of the lips of whom fifty-seven or 48 per cent. were heavy smokers. There were thirty-three patients with cancer of the mouth of whom nineteen or 58 per cent. were heavy smokers. There were nine patients with cancer of the palate, and fifty-three with cancer of the tongue of whom thirty or 57 per cent. were heavy smokers. Among twenty-six patients suffering from cancer of the tonsils, thirteen or 50 per cent. were heavy smokers. Among sixty-eight patients with cancer of the œsophagus, thirty-four or 50 per cent. were heavy smokers. There were only three patients with cancer of the pharynx and five with cancer of the throat. There were thirty-seven patients with cancer of the larynx, of whom sixteen or 43 per cent. were heavy smokers. Finally, there were twenty-seven patients with cancer of the lungs, of whom eighteen or sixty-seven were heavy smokers. These wide variations are highly suggestive of the need of a much larger collection of facts for definite conclusions. But they are unquestionably indicative of a greater liability to certain forms of cancer among those who have acquired heavy smoking habits than among those who indulge normally. But as I have said before, it is extremely difficult to make sure that the statements regarding the habit are nearly accurate or measurably reported.

The foregoing results are strictly comparable with corresponding figures for non-cancer patients in San Francisco. These were patients suffering mostly from chronic diseases of adult life, chiefly heart diseases, arteriosclerosis, arthritis, hypertension, diabetes, nephritis, etc. I secured this information for 537 male patients and of these 236 or 42.3 per cent. reported themselves as heavy smokers against 45.6 per cent. for cancer patients and 47.3 per cent. for patients suffering from cancer of the buccal cavity. The differences are therefore very slight, which may be construed as opposed to the theory that smoking habits increase materially the liability to malignant tumors, particularly of the buccal cavity, œsophagus, larynx and lungs, but I would be reluctant to draw such a conclusion. Smoking habits may possibly constitute but one of a number of factors which must enter into the development of malignant tumors, the absence of any one of which might preclude such a development. Unfortunately the subject has not been studied as thoroughly as its importance would justify. But the observed excess in cancer of the buccal cavity in men, as well as in cancer of the œsophagus and the lungs, is highly suggestive of the influence of smoking habits, however difficult it may be to establish this conclusion statistically.

In the United States, among the white male population, in 1927, 5.8 per cent. of the cancer deaths were from cancer of the buccal cavity. For negroes this proportion was 5.6 per cent. and for Indians 5.5 per cent. For

Chinese it was only 2.3 per cent., which is highly suggestive since the Chinese are rarely addicted to heavy smoking habits. Now when these averages are compared with other countries, there appear some very surprising differences. The highest known proportion which I have been able to ascertain is for the white male population of Cuba, 1918-1922, or 14.6 per cent. This is followed by the male population of Mexico for 1928 with 13.8 per cent. Next in the order of importance comes the colored male population of Cuba with 11.7 per cent. This is followed with 10.8 per cent. for Australia, 1927, 10.3 per cent. for England and Wales, and the same figure for Scotland for the year 1928, and 10.4 per cent. for the European population of South Africa, 1922-1926. All these are measurably in excess of our American proportions. For New Zealand the proportion was 4.4 per cent.; for Shantung, China, Hospital, 1923-1926, 5.1 per cent.; for Buenos Aires, 1925, 7.9 per cent.; and for Canada, 1922-1928, 7.8 per cent.

Figures more nearly approaching those of the United States are those of Spain 1926, 7.3 per cent.; Manila, P. I., 1924-1925, 6.6 per cent.; Paris, 1924, 5.4 per cent.; Hawaii, 1924-1928, 3.7 per cent.; Holland, 1927, 3.5 per cent.; and Japan, 1924-1928, 3.4 per cent. This is the lowest figure of which I have record except for the Chinese of the United States, for whom, however, the numbers are very small.

Throughout the international comparison females invariably have a lower proportion of cancer of the buccal cavity than males, except the females of Manila. Here the proportion for 1924-1925 was 10.2 per cent., ascribed to the betel nut chewing habit, which includes tobacco and which is a direct causative factor in the development of cancer of the mouth, as also observed in Ceylon and South India. I would like to have given some additional figures for Egypt but unfortunately the sex was not separated in the return furnished me by the Egyptian Government. But out of 991 cases of cancer, all forms, during 1927-1928, 136 or 13.6 per cent. were cancers of the buccal cavity. The proportion therefore is relatively high.

In the United States in 1927, cancer of the buccal cavity for both sexes combined formed 3.1 per cent. of the total mortality from cancer. This is based on 3,184 deaths, of which 487 were deaths from cancer of the lip, 829 cancer of the tongue, 372 cancer of the mouth, 1,054 cancer of the jaw, and 442 from others of this class. In other words, a considerable proportion of deaths from cancer of the buccal cavity was from cancer of the jaw and others in this class, numbering in the aggregate, 1,496 or nearly one-half the total. Mortality from cancer of the buccal cavity represents types of malignant tumors in all probability very slightly connected with smoking habits. Cancer of the pharynx caused 1,044 deaths, or a rate of 1 per cent. of the total mortality from all forms of cancer, and cancer of the larynx caused 779 deaths, or 0.8 per cent. Cancer of the lungs and pleura caused 2,012 deaths, or 1.9 per cent. In addition, cancer of the œsophagus caused 1,756 deaths or 1.7 per cent. If, therefore, we combine the different forms of cancer most generally assumed to bear a direct relation to smoking habits,

it appears that out of a total mortality from cancer of 103,578, 7,229, or 7.0 per cent., were attributable to the seven organs or parts in all probability most affected by smoking habits, a very substantial proportion well deserving of further and more extended consideration.

Indirectly the problem may be approached in another way. Smoking habits, unquestionably, during the last ten to fifteen years have increased enormously in this country until the practice has become almost universal among men, while it has been extended to women to an extraordinary degree. This practice refers chiefly to cigarette smoking, however, which by common consent is considered less harmful than pipe and cigar smoking as an irritant to the buccal cavity and the upper respiratory tract and possibly the lungs. I therefore examined into the deaths reported for different forms of cancer since 1915 with the following results:

Cancer of the lip in the registration area has remained stationary, prevailing at the rate of 0.5 per 100,000 in 1915, and 0.5 in 1927, rising in only one year to a rate of 0.6. Since pipe smoking and heavy cigar smoking has diminished during this period this result is not unexpected. Cancer of the tongue prevailed at a rate of 0.8 per 100,000 in 1915, and at the same rate in 1927. Occasionally the rate has gone down to 0.7 and in a few years it has risen to 0.9, but on the whole the rate has been practically stationary during the period under review. Here again also is evidence that the decline in the heavier types of smoking has left the situation of fifteen years ago practically unchanged. Cancer of the mouth prevailed at a rate of 0.4 per 100,000 in 1915, and 0.4 in 1927. During some years the rate has gone down to 0.3, but on the whole it has been practically stationary during the entire period under review, confirming previous observations with regard to cancer of the lips and tongue. For cancer of the pharynx unfortunately no trustworthy data are available until 1922. In that year the rate was 1.2 per 100,000 while in 1927 it was 1.0. Again the situation regarding this type of cancer conforms to that previously shown for cancer of the lips, tongue and mouth.

But when we consider cancer of the œsophagus, it appears that the rate has increased from 1.0 per 100,000 in 1915 to 1.7 in 1922. During the last six years, however, the rate has gone down, falling to 1.4 in 1924, rising to 1.6 in 1925 and 1.8 in 1926, but declining again to 1.7 during 1927. While therefore the rate is materially higher during the last eight years compared with 1915, it remains almost unchanged during these eight years although smoking habits have increased enormously. But it must always be kept in mind that the increase in smoking habits affects the different forms of smoking of cigarettes instead of the earlier and more common method of smoking pipes and heavy cigars.

Cancer of the larynx prevailed at the rate of 0.5 per 100,000 during 1915, rising to 0.7 in 1922 and 0.8 in 1923. It has remained at that figure year after year until 1927. Comparing the first year with the last there has been an increase but not sufficiently pronounced to be considered alarming.

When we come to cancer of the lungs, however, the rate starts with 0.7 per 100,000 in 1915, rising to 1.1 by 1920 and to 1.6 by 1924, and reaching a maximum figure of 1.9 in 1926 and the same figure for 1927. This increase in cancer of the lungs is by many authorities attributed rather to improved diagnosis than to a greater liability of the lungs to malignant diseases. This point of view I would be reluctant to accept. I am strongly inclined to think that the increase is directly connected with the much wider spread of cigarette smoking habits, including the inhaling of smoke which must enter the lungs to a considerable extent in many cases. But this would not be the only factor accounting for the increase, for there may possibly be a connection with the gross air pollutions of large cities as the result of motor cars. It is certainly significant, however, that out of seven types of cancer more or less connected with smoking habits, cancer of the lungs should at the present time show a higher mortality figure, or to be precise, in the order of importance, the lowest figure is for cancer of the mouth, or 0.4, followed by cancer of the lips, or 0.5, cancer of the tongue, 0.8, and the same for cancer of the larynx, cancer of the pharynx, 1.7, and cancer of the lungs, 1.9.

I have extended this analysis to England and Wales, for which standardized figures are available since 1901. The statistics for England and Wales, however, are for males only and must therefore not be confused with the corresponding figures for the United States registration area which are for both sexes combined. Cancer of the lips in England and Wales increased from 1.3 per 100,000 in 1901-1910 to 1.6 in 1926, declining to 1.2 during 1927. Cancer of the tongue remained practically unchanged, prevailing at the rate of 4.3 at the beginning of the period, rising to 5.1 during the next ten years ending with 1920, but declining to 4.4 in 1926 and 4.3 in 1927. For cancer of the mouth figures are available only since 1911. These show an increase in the rate from 2.4 per 100,000 at the beginning of the period of 3.0 during 1926 and 3.0 for 1927. Cancer of the pharynx increased from 1.1 during 1911-1920 to 1.3 during 1927. Cancer of the œsophagus increased slightly from 5.1 during 1901-1910 to 5.5 during 1911-1920, 6.5 during 1926 and 6.1 during 1927. Cancer of the larynx increased from 2.4 per 100,000 during 1911-1920 to 3.4 during 1926 and 3.2 during 1927. Cancer of the lungs increased from 1.0 per 100,000 during 1901-1910 to 1.3 during 1911-1920, with a much more decided upward tendency to 2.3 in 1926 and 2.3 during 1927. In a general way, therefore, the English figures confirm those for this country, but unfortunately they are not strictly comparable since the English figures are standardized for age variations during the years under review, while at the same time they are for males only, the combined figures for both sexes not being available. But they justify the assumption that cancer of the lips, tongue, mouth, œsophagus and larynx are unquestionably very much more common in England and Wales than in this country.

To make this point clearer, I am able to give comparable rates for cancer of the buccal cavity, considered as a group, for the two countries. In

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1927 the death rate from cancer of the buccal cavity for both sexes combined was 3.5 for the United States registration area against 8.0 for England and Wales. In 1920 the corresponding rates were 3.5 for the United States and 7.5 for England and Wales. It therefore admits of no controversy that cancers of the buccal cavity, considered as a group, are enormously more common in England and Wales than in this country. It is doubtful whether smoking habits are any more common on the other side of the Atlantic than on this; but I think it is a fair observation that Englishmen are much more addicted to pipes and cigars than Americans, who are more addicted to the cigarette habit. As I have previously shown, the proportion of deaths from cancer of the buccal cavity in the total mortality from cancer, all forms, was 10.3 per cent. for England and Wales against 5.8 per cent. for the white population of this country. The statistics are therefore apparently conclusive, but nevertheless suggestive of a much more extended study of all the facts of the situation bearing particularly upon the six points raised at the outset of the present discussion, every one of which bears upon the variations in the incidence observed. The method followed in my questionnaire examination of cancer patients if enlarged upon with particular regard to cancer and smoking habits would therefore in my opinion yield excellent results if pursued on a larger scale with due regard to international conditions than has been possible in connection with the San Francisco Cancer Survey.

Research in the literature of the subject has failed to bring forward extended observations on the subject. But I have not access to all the standard works on cancer in the different languages which might have proven productive of useful information at present unknown to me.

As regards cancer of the lips, Sir John Bland Sutton observes that "It is remarkable that though men are so much more liable to cancer of the lower lip than women, yet the liability is equal for both sexes in regard to the upper lip. Out of the thirty-one cases of cancer in the upper lip in Loos' total of 565, sixteen occurred in men and fifteen in women. The increased liability of men to cancer of the lip as compared with women is attributed to the greater frequency of tobacco smoking among men. In connection with this matter it may be mentioned that cancer of the lip is sometimes spoken of as 'countryman's cancer,' on account of the frequency with which it occurs among agricultural laborers, who use short-stemmed dirty pipes. The clay pipes with short stems are very convenient, as they can be carried in the pocket. In London hospitals some patients with cancer of the lip are farm laborers, but many are men who come under the term 'laborers' and their custom in regard to the short pipe is the same as the farmhand's. The stem of a short clay pipe soon becomes hot when in use, and burns or scorches the lip. Chronic ulcers caused by burns are prone to be the starting-points of squamous-celled cancers."

There are many other interesting observations by Sir John Bland Sutton which should not be overlooked. I can quote only the following, that "Cancer is occasionally seen in the lips of patients who do not smoke tobacco.

and who are not tainted with syphilis." This is precisely the point I would like to emphasize in the correlation of smoking habits to cancer of the buccal cavity and other parts of the body and upper air passages, that not all this mortality can by means be charged to smoking habits, and possibly only a small fraction. I regret that I have no data whatever for cancer of the upper or lower lip for this country since the facts are not taken cognizance of in the mortality returns. I add to the foregoing a brief quotation from an interesting discussion on cancer of the lip by William H. Kennedy, Indianapolis, published in *Radiology*, April, 1925. Doctor Kennedy observes that "The etiological factors in the production of this condition are still causing considerable discussion in all quarters. Although the use of tobacco-pipe smoking especially has long been regarded as being chiefly responsible for the appearance of the lesion in this particular locality, a sufficient number of cases have occurred in persons who never use tobacco to disprove this theory. And whereas smokers' burn has been given a prominent place in the etiology of cancer of the lip—benign in the beginning but later developing into a malignancy—the writer's personal experience leads him to conclude that the importance of tobacco in the causation of this condition has been overemphasized. In examining the histories of the 150 cases on which this article is based, it has, therefore, been concluded that the predisposing causes are undoubtedly of a complex nature and that no single agent can be held exclusively responsible for this malignant state of the lip nor of the cancerous condition elsewhere in the human organism." Doctor Kennedy, however, fails to draw the marked distinction insisted upon by Sir John Bland Sutton as regards the particular liability of the lower lip and its relation to pipe-smoking habits.

I have a brief note from the *Annals of the Faculty of Medicine of Montevideo*, December, 1925, in which there is an extended discussion on cancer of the lip by Dr. Carlos Butler, summarized in the statement, "Butler analyzes 173 cases of cancer of the lip and eighteen of pre-cancer conditions. In the 159 cases involving the lower lip, seventy-seven were smokers and fifty-one maté users. The total 191 cases included 8.8 per cent. women; in 23.2 per cent. the lesion was a post-operative recurrence. Under radium treatment, 60.3 per cent. were clinically cured and only 10 per cent. showed no improvement, in the lower lip cases, while 81.8 per cent. were cured and 18.19 per cent. improved in the upper lip cases."

Cancer of the tongue, in all probability, is only in rare instances connected with smoking habits. The etiological factor is more likely to be defective dental conditions often complicated by syphilis and resulting leucoplakia. Many years ago Sir D'Arcy Powers called my attention to syphilis in connection with cancer of the tongue, holding the opinion that he rarely saw a case in which syphilis was not present. Charles Ryall is quoted by Hastings Gilford to the effect that he had collected figures showing the relation of syphilis to cancer of the tongue and found that in over 80 per cent. of the cases cancer took place in a syphilitic subject. The same writer

quotes Poirier's views that "Everybody cannot have cancer of the tongue; two conditions are almost indispensable—you must be a smoker or syphilitic; and those who combine those two conditions, especially the latter, have a much greater risk than other people. Cancer of the tongue might be called the cancer of syphilitic smokers."

Gilford Hastings, in discussing the question, remarks that "Tobacco acting as a strong local irritant is one of the sources of tongue cancer. Thus the causes of the leucoplakia which precedes cancer of the tongue are, according to Barker, 'Frequent abuse of alcohol, of spices, hot foods, and undoubtedly tobacco smoke' Leucoplakia was at one time termed 'smokers' tongue. Those who chew tobacco are also liable to this form of cancer, and Ewing says that these cancers often develop at the point where the quid is held. In Gibraltar and among the Spaniards of the neighborhood cancer of the tongue and lip is very common, and is attributed by Turner, of the Colonial Hospital, to excessive cigarette smoking."

Cancers of the lip and tongue are, of course, subject to remedial treatment and the mortality figures must be considered affected by the results of such treatment which to an increasing extent are suggestive of a hopeful outcome. Radiology in this respect has made immense progress with encouraging prospects for the future.

In my "Mortality from Cancer Throughout the World," in discussing the cases treated at the New York State Institute for Malignant Diseases, I give a number of illustrative cases showing, for example, that for cancer of the lip there were twenty-two deaths at an average age of seventy-four years in which smoking was the probable cause of fourteen. Other causes alleged were a cut on the lip in one, ulcer of the lip in another, a wart in the third, and a tooth in a fourth. There was a personal history of alcohol in three cases, of syphilis in only one. I give an analysis of twenty-three deaths from cancer of the tongue at an average of sixty-eight years, in which the probable cause was smoking in twelve, irritation from a tooth in three, while there was a personal history of alcohol in six, and syphilis in only one. There were four female deaths from cancer of the tongue in which the probable cause was given as smoking in one. The Gibraltar case is mentioned in my "Mortality from Cancer Throughout the World," being derived from the Colonial Office correspondent in connection with the Imperial Cancer Research Scheme. In this it is said: "Probably three-fourths of all cases of cancer met with in the practice of the Colonial Hospital, have their seat in one or the other of these organs. The predisposing causes of cancer, in this part of the world, appear to me to be, in males, excessive tobacco smoking, leading to irritation of the lips and tongue; in females, premature child-bearing and lactation. The Spaniard's cigarette or cigar is never absent from his lips if he can help it, and he allows it to burn so close that the actual fire must frequently char the epithelium of his mouth."

I have shown previously that cancer of the buccal cavity in Spain caused 7.3 per cent. of the total deaths from cancer against 5.8 per cent. for the white



population of the United States and 14.6 per cent. for the white population of Cuba, where the population, as in Spain, is likewise addicted to excessive smoking habits. The same is true of Mexico City where the proportion is 13.7 per cent. or the second highest in the international compilation previously dealt with. It is highly significant that in Cuba among the white female population, cancer of the buccal cavity should be as high as 4.9 per cent. against 1 per cent. for the female white population of the United States and 6.1 per cent. for the colored female population, while it is 4.5 per cent. for the female population of Mexico City, and for Spain in marked contrast, the proportion is only 1.5 per cent. but still markedly higher than for the white population of this country.

Cancer of the œsophagus is such a serious affection that changes in the death rate during recent years are not very likely to reflect to any measurable degree improvements in treatment. The affection was the cause of 1,756 deaths during 1927 in the United States registration area, equivalent to a rate of 1.6 per 100,000, or 1.7 per cent. of the total mortality from all forms of cancer. Since 1915, as I have had occasion to point out, the rate has increased from 1.0 to 1.7. In England and Wales the actual mortality from cancer of the œsophagus has increased from 5.1 per 100,000 for males to 6.1 between 1901 and 1927. The disease is therefore decidedly more common in England and Wales than in this country even though precise figures for comparison for males only are not available. The œsophagus, according to Cunningham, "is the narrowest and at the same time one of the most muscular of the alimentary tubes." Being extremely narrow it is therefore subject to no end of irritation during the process of alimentation, giving rise no doubt to numerous causative conditions favorable to malignant growths. The relation of smoking habits to cancer of the œsophagus must therefore in all probability be one of many factors explaining the relatively high incidence of this affection in males, who suffer decidedly more than women. While the death rate for cancer of the œsophagus is 6.1 per 100,000 for males in England and Wales, it is only 1.5 for females, or about the same rate as prevails for both sexes combined in this country. For females in England and Wales the rate has increased from 1.5 in 1901-1910 to 1.8 during 1927. This might possibly be related to the immense increase in smoking habits in England among women during recent years.

Dr. William Hill some years ago, in a discussion before the Royal Society of Medicine, pointed out that the statistics of cancer of the œsophagus have been falsified by the inclusion of many cancers of the pharynx. This in all probability has been the case in this country previous to 1922 on account of which I have not used the statistics of cancer of the pharynx for the earlier years in my comparison. If this explanation is accepted, deaths from cancer of the œsophagus in this country have increased probably much more than the indicated growth in the rate from 1.0 in 1915 to 1.7 in 1927. That this increase is, in part at least, attributable to smoking habits cannot be denied although the positive evidence may be wanting. In the etiology of

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cancer of the œsophagus, much more stress is generally placed upon hot foods and hot drinks, or alcoholic drinks, than upon smoking. Fischer, in the *Clinical Weekly* in 1924, makes reference to the alleged frequency of cancer of the œsophagus in the Chinese and the view that it was due to the eating of hot rice, but this view he rejects. He observes, however, with regard to the etiology of cancer of the œsophagus that, "There are many facts in favor of the view that it is excited by chronic irritation." He adds that "Cancer is most liable to develop at the three points where the œsophagus is narrowest. The disease is much more common in men than in women. The influence of alcoholic excess has been much disputed. In Argentina the disease has been regarded as the result of drinking very hot 'maté'; in China the drinking of hot arrack has been regarded as an exciting cause." In this he does not mention smoking at all and leaves the situation as confused as before.

Somewhat earlier, in the *British Medical Journal* of December 8, 1923, Dr. William Hill, London, attributed cancer of the œsophagus primarily to excessive drinking of concentrated forms of alcohol or of excessively hot fluids. Here he observes in this connection that "In my investigations the number of those individuals who were found to be the victims of cancer of the œsophagus who gave a clear history of excessive drinking of either ardent spirits or very hot fluids or both has not been such as to impress me with the correctness of alleged association implying cause and effect." He also leaves the confused situation unchanged. It is significant that he should make no mention of smoking habits. An extended discussion of cancer of the œsophagus by Dr. J. Guisez of Paris, at the University of London, in 1924, fails to mention tobacco as an exciting cause, although mentioning chronic irritation of alcoholic origin. Mention may be made of a statement by Ropke, a German authority, according to which there are twenty-three cases of cancer of the œsophagus in men to three in women, and that he believes that this disparity is due to the influence of alcohol and tobacco. With this statement I concur.

In cancer of the larynx it is reasonably certain that smoking habits play an important part. In the British figures the mortality from cancer of the larynx is given as 3.17 per 100,000 for men and as 0.7 for women. Hence we have here the same decided disparity between the two sexes as observed in cancer of the œsophagus and buccal cavity. Many of those who have written on the subject have attributed to smoking habits direct causative results in cancer of the larynx but I am not aware of any exhaustive study from a statistical point of view. Most of the references available to me are of no particular value in supporting the conclusion one way or the other. I, however, can see no reason why the larynx should not be particularly susceptible to the irritating effects of tobacco smoking, granting that the latter is productive of cancerous affections.

In cancer of the lungs the effects of tobacco smoking are more difficult to prove but there is not the slightest question of doubt as to the fact that those who practise inhaling certainly drive the smoke into the innermost

recesses of the lungs. The observed increase in cancer of the lungs during recent years is highly suggestive of its correlation to the immense spread of cigarette-smoking habits. In the English statistics the mortality from cancer of the lungs for 1927 was at the rate of 26.8 for men and 9.7 for women. Here again the disparity in sex susceptibility is highly suggestive of smoking habits as a causative factor. But cancer of the lungs has been attributed to a variety of modern conditions which may account more or less for the observed increase which cannot be entirely, at least, attributed to better diagnosis. In England and Wales cancer of the lungs has increased in males from 0.2 during the ten years ending with 1910 to 26.8 during the year 1927. In females the rate has increased during the same period from 7.0 to 9.7. Yet smoking habits have proportionately increased faster among women during recent years than among men. But the fact must not be lost sight of that the injurious effects of tobacco smoking in their relation to cancer probably require quite a long period of time to become noticeable. Since I have dealt with the question of cancer of the lungs in a separate discussion published in the *American Journal of Tuberculosis*, I will not enlarge upon it on this occasion, except to say that personally I am strongly of the opinion that a relation between the increase in smoking habits and cancer of the lungs may safely be assumed to exist. I have never been inclined to accept the view that the increase in lung cancers during recent years is chiefly attributable to the after-effects of the influenza epidemic. As observed in the *Journal of the American Medical Association* of February 13, 1926, the clinical records in a large proportion of the investigated cases did not show any history of influenza.

How far smoking habits may affect other organs and parts in their specific liability to cancerous affections involves difficulties which do not admit of being dealt with on this occasion. I am full well aware that there are those who maintain that the increase in cancer of the stomach bears some relationship to smoking habits.

Lickint, among others, has advanced the following conclusion: "Nicotin decreases the action of pepsin and of rennet. Potassium sulphocyanate, found in excess in the saliva of smokers, has an inhibiting effect on protein digestion. In chronic smokers, the peristalsis is first increased, later decreased." He therefore believes: "Tobacco may play an etiologic rôle in neuroses of the stomach, in disturbances of its secretory function, in gastritis, and even in ulcer and cancer."

But so many factors enter into gastric cancers that it is extremely difficult to isolate the pronounced effects of any one particular factor in a satisfactory manner. I shall presently consider some more extended observations of Lickint in his most recent contribution to the *Journal of the German Society for Cancer Research* in which he covers the entire field, although in rather a superficial manner, but amplified by a large number of references extremely useful to the research student.

Before I consider these observations I would like to emphasize briefly

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certain additional aspects of the cancer problem generally overlooked. The natural duration of cancer has been subject to much discussion though rarely dealt with on the basis of adequate data. In the nature of the case the natural or known duration of the disease can at best represent but a scientific guess upon a more or less confused state of facts. The onset of cancer is too obscure in the human body to permit of being determined, except in rare cases of trauma, with absolute precision. I have therefore used the term "known duration of cancer" as given on the death certificate by the attending physician. Since cancer is not a painful disease at the onset, more or less conjecture enters into every individual determination of disease duration. In my San Francisco Cancer Survey I have tabulated the known duration of the disease for a large number of organs and parts and in most cases on the basis of a fairly large number of observed cases. Selecting fourteen different organs and parts for purposes of comparison, the known duration of the disease in all my tabulated deaths for different localities and sections of the country, including eight years of observations in San Francisco, has been as follows: The known duration, previous to death in males, was longest in cancer of the lip, or 25.1 months. This was followed by cancer of the prostate with 20.3 months and cancer of the bladder with 17.5 months. It was 16 months in cancer of the rectum, 14.9 in cancer of the tongue, 14.9 in cancer of the liver, 13.9 in cancer of the intestines, 13.6 in cancer of the jaw, and the same or 13.6 months in cancer of the stomach, 12.8 in cancer of the larynx, 10.1 in cancer of the lungs, 9.3 in cancer of the œsophagus and 9.0 in cancer of the pancreas.

These are the statistics for male deaths only for American cities. For certain Canadian Provinces and cities the results on the whole fairly conform to those for the United States, particularly cancer of the lip, which shows an average known duration of 26.7 months, followed by cancer of the bladder with 18.5 months. But the Canadian returns are numerically less trustworthy. Hence in estimating the effects of the growth of tobacco smoking, some allowance must be made for the probably much longer natural duration in cancer of the lips, as, for example, compared with cancer of the tongue, œsophagus and the lungs. But in any event, the known duration of the disease before death is at best but a matter of conjecture however well statistically established. The known duration of the disease previous to death must not be confused with the known duration previous to the time the patient received his first medical attention. It would seem, however, that the duration in no case is sufficiently long to offset the prodigious rise in tobacco consumption in this country during recent years.

In an address on "The Causal and Formal Genesis of Cancer," read by Doctor Ewing at the London Cancer Conference in 1928, occurs the remark: "One will hardly err in accepting the conclusion of the older clinicians that cancer of the mouth would disappear if tobacco, bad teeth, and syphilis could be eliminated." In his earlier address at the Mohonk Conference in 1926 Doctor Ewing said: "Among preventable cancers the most obvious is the

intra-oral group. It has long been known that cancers of the lip, mouth, tongue and tonsil are due to bad teeth, tobacco and syphilis and the importance is, I think, in the order named. Experience in a large clinic for these diseases reveals, on the average, an astonishing degree of irritation due to these factors." And in continuation, "Cancer of the lip is nearly always caused by the irritation of tobacco but a prominent predisposing factor is seborrhœic dermatitis and inflammation of the vermilion border. . . . The use and especially the abuse of tobacco must be charged with a large share in the production of intra-oral cancer as well as of cancer of the larynx and probably of the œsophagus." Finally he remarks: "One may hardly aim to eliminate the tobacco habit, but cancer propaganda should emphasize the danger signs that go with it."

While there is apparently a reasonable consensus of qualified opinion as to the injurious effects of heavy smoking habits, no light is thrown upon the real nature of the problem as modified by various considerations to which I have drawn attention at the outset, for the changes in smoking habits have introduced forces, the effect of which it is difficult, if not impossible, to measure. Dr. W. Blair Bell, of Liverpool, for example, has expressed the opinion: "Cigarettes, without holders, and cigars were not so dangerous, because they were held in all parts of the mouth. But in the case of pipes and cigarette-holders it was found that the stem could be held in the mouth most comfortably in one particular position. The result was that over a period of years a hot stream of smoke was directed on to a particular part of the mouth or tongue, producing an irritant sufficient to account for the precancerous condition." The habit of using cigarette-holders as yet is rather rare. Most men smoke cigarettes without holders, but in many cases they smoke the cigarette too near to the mouth so that a burning sensation can be distinctly felt. In the case of cigarette-holders there is much variety of varying degrees of heat conductivity. The difficulty with many cigarette-holders is that they permit the cigarette to be smoked to the very limit of combustion, thus probably increasing the degree of heat which reaches the membranes of the buccal cavity, much more so than in ordinary cigarette-smoking habits. Unless regard is paid to this factor a correct answer to the question as to how far smoking habits are causative factors in buccal cavity cancers, or cancers of the œsophagus and larynx, as well as of the lungs, is not likely to be forthcoming. But there is the further implication of most of the authorities, that in the absence of syphilis, and in the absence of serious dental defects, smoking habits, even if carried to excess, are much less liable to produce cancers than in the presence of the conditions just mentioned. Thus Sir Bruce-Porter gives expression to the view that:

If you use tobacco in moderation, it is not going to do you any harm. Some people cannot smoke and they should leave tobacco alone. If you can prevent boys from fourteen to eighteen smoking, you will be doing a good thing, and then you can let them smoke from eighteen to eighty. Tobacco is an extraordinary comfort to a great many people, who should not be terrified from enjoying one of the few joys that remained to people of advanced years. Extremes should be avoided in either direction.

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Moderation in smoking, commenced in adult life and carried on with reasonable safeguards is, in all probability, free from serious danger, particularly in the absence of syphilis and dental impairments. If this were not so, the immense increase in cigarette smoking would unquestionably have been productive of a decided increase in cancers of the specific organs and parts most affected by smoking habits. I will review once more some of the evidence as to smoking habits which have a direct bearing upon fluctuations in the cancer death rate. Heavy pipe and cigar smoking has materially diminished during the last decade. The amount of tobacco used for smoking purposes has increased only from 228,000,000 pounds in 1919 to 231,000,000 pounds in 1928 regardless of the very substantial increase in the meantime. Consumption of chewing tobacco has materially diminished, particularly plug tobacco, from 141,000,000 pounds in 1919 to 100,000,000 in 1928. Curiously enough, however, the use of snuff has increased from 35,000,000 pounds in 1919 to 40,000,000 in 1928. Heavy cigar smoking has diminished from 7,000,000,000 in 1918 to 6,400,000,000 in 1928. Light cigar smoking has diminished from 700,000,000 in 1919 to 415,000,000 in 1928. The consumption of heavy cigarettes has diminished from 32,000,000 to 10,500,000, but the consumption of light cigarettes, or those weighing not more than three pounds per 1,000, has increased from 53,000,000,000 in 1919 to 108,000,000,000 in 1928. In other words this enormous increase in smoking habits has not been accompanied by an equal increase in tobacco consumption. The total amount consumed has increased only from 648,000,000 pounds in 1919 to 754,000,000 pounds in 1928.

Much to my regret I am unable to give absolutely trustworthy data on per capita consumption of different countries, being of the opinion that most of the published statistics fall short of intrinsic accuracy, in view of the confusion of terms. *The Norwegian International Yearbook* for 1928, for example, gives the per capita consumption of tobacco for the United States as having been 3 kilograms in 1913 and only 2.7 kilograms in 1927. But I do not think this is in strict conformity to the facts. But this consumption is the highest given for any country in the world tabulated by the Norwegian government, except Holland, which shows a per capita consumption of 3.5 kilograms in 1913 and 3.2 kilograms in 1926. Yet these two countries have by no means the highest proportionate figures for cancers of the buccal cavity, which are exceeded by those of England and Wales. Unfortunately, the tabulation does not include statistics for Cuba, which shows the highest proportion of deaths from cancer of the buccal cavity of the various countries dealt with previously, nor for Mexico City and Spain. However, the data on the subject are highly suggestive of the value of a thoroughly specialized study on the whole question which must needs profoundly affect the world's population addicted to smoking habits. In its last analysis, the actual number of persons who suffer from cancerous affections as the result of tobacco smoking is but a small proportion of those who actually practise the habit, yet the situation is sufficiently serious to demand public education along the

line of least liability, since the habit once acquired is very difficult to be gotten rid of.

The whole question of tobacco smoking as a causative factor in cancer has very recently been reviewed by Dr. Fritz Lickint, of the City Hospital of Kuckwald, Chemnitz, published in the *Proceedings of the German Society for Cancer Research*, 1929 (vol. xxx, Part 4). Doctor Lickint reviews the entire literature on the subject, quoting 167 authorities, suggestive of the vast amount of attention that has been given to the subject, but regrettably, in most cases limited to individual objective findings in a comparatively small number of cases. Lickint, however, arrives at the correct conclusion that the irritating factor of tobacco and tobacco smoking is a complex one. For aside from chemical effects, there are mechanical and caloric effects of smoking which cannot be ignored. He reports results of animal experimentations of great interest but too technical to be reviewed on this occasion. He makes one important observation and that is the absolute absence of skin cancers of the hands and fingers as the result of cigarette-smoking habits particularly in the manipulation of tobacco during manufacturing processes. According to the most recent statistics by Dublin on "The Causes of Death by Occupation," published in February, 1930, by the United States Bureau of Labor Statistics, cigar smokers and tobacco workers show a standardized relative index of cancer of 118.

Lickint confirms the observation that pipe smokers and heavy cigar smokers generally suffer most from cancer of the lower lip, which may be accepted as conclusive evidence of cause and effect. He draws attention to the practical absence of lip cancers in glass blowers and musicians using metal instruments which must involve a considerable degree of lip irritation. He includes some extremely interesting temperature observations on cigarette smoking which are also too technical to be enlarged upon but which are suggestive of a direction in which further research would be extremely valuable. He arrives at the same conclusion as Ewing that the discontinuance of smoking habits would unquestionably result in the disappearance of many of the cancers to which men at the present time are curiously liable. Lickint also endorses the view that syphilis and cancer of the tongue are in most cases closely associated and that syphilitics should absolutely discontinue smoking habits. He goes further, however, and attributes a certain proportion of deaths from cancer of the stomach to smoking habits, and of being particularly productive of ulcers of the stomach on the part of those who practise the habit of smoke inhalation. He agrees that smoking habits have a close relation to bronchial and lung cancers, attributing the increase in this form of cancer to smoking habits, particularly cigarette-smoking habits during recent years.

Summarizing the foregoing rather extended observations on one of the most important phases of the cancer problem, the following conclusions would seem admissible:

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1. Smoking habits unquestionably increase the liability to cancer of the mouth, the throat, the œsophagus, the larynx and the lungs.

2. The change in the cancer death rate during recent years has not, however, been at all disproportionate to the enormous increase in cigarette-smoking habits, which have replaced the older method of smoking, unquestionably more injurious than the smoking of cigarettes.

3. The problem is complicated by other factors, particularly syphilis and defective dental conditions, in the absence of which, smoking habits are much less likely to result in cancerous affections.

4. The increase in cancer of the lungs observed in this and many other countries, is, in all probability, to a certain extent directly traceable to the more common practice of cigarette smoking and the inhalation of cigarette smoke. The latter practice unquestionably increases the danger of cancer development.

5. In the absence of other predisposing conditions, extreme moderation in smoking habits would certainly be advisable. Likewise attention requires to be given to the use of cigarette-holders and cigar-holders of a high degree of conductivity which must needs increase the liability to cancerous affections.

6. Finally something should be said as to the gross amount of air pollution as the result of almost universal smoking habits, which may in some cases injuriously affect non-smokers who are the victims of conditions over which they have little control. This observation applies particularly to the development of cancer of the lungs which occur among women, as well as among men, and frequently among those who are not smokers.

Even the most exhaustive study of the present state of knowledge regarding smoking habits in their relation to cancer leaves many of the most important questions unanswered. There is, therefore, the utmost urgency for qualified research into what is still a rather obscure aspect of the larger problem of cancer control, and it is to be hoped that the present study will be of some aid in this direction and stimulate more qualified research workers to subject the data and conclusions to a competent analysis.



# THE RÔLE OF LYMPH STASIS IN THE GENESIS OF CANCER

THE EVIDENCE OF LYMPHANGITIS IN PAPILLOMATA

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IN LAYING before my American colleagues some further evidence in favor of the view of the origin of cancer with which my name is associated, the view, namely, that cancer is a product of lymph-stasis, I desire not only to do honor to the great master of morbid histology to whom this volume is a tribute but also to give an additional proof, if such were needed, of the unexhausted possibilities of the study to which he has given his life. In the earlier part of my professional career morbid histology—in England at any rate—was regarded as *vieux jeu*, an exhausted and closed subject completely embodied in textbooks and from which nothing more could be hoped. The revival of interest in it has of late made great progress, and it is now holding its own with its younger rivals in the field of pathology such as bacteriology and bio-chemistry, and is advancing by equal steps with them. It is claiming, as much as other branches of pathology, the exclusive devotion of able young men, though in many universities and medical schools it is still inadequately recognized and endowed. It cannot be doubted that the improved position of the subject is largely due to Professor Ewing and to that great piece of organization, his work on "Neoplastic Diseases."

The evidence that cancer arises in districts where for long years there has been a local lymph-stasis, impairing the nutrition of the cells, was first stated in a paper read before the Interstate Post-graduate Convention at Cleveland in 1926.\* On that occasion I was able only to state the subject in its bare outlines, and though I have returned to it since in an address given in Wellington, New Zealand, last year,† and in a recent Hunterian lecture, at present unpublished, given at the Royal College of Surgeons of England, there is still much to be said upon it. Nothing has encouraged me to pursue the subject so much as a letter received from the senior surgeon of the world, Professor W. W. Keen, in which he says, "I have just read your very interesting address on 'Lymph-stasis the Precursor of Cancer.' It appeals to me as the most reasonable and almost certain paper on the origin of cancer that I have ever seen. All others are guess work. Here is a series of facts—observations which cannot be disputed. I hope you will follow it up and be able to establish the doctrine on most solid ground. I think it gives us more nearly the origin of cancer than any other paper I have seen. Whether we can do anything to prevent or remedy the stasis of the lymph or not is the next question. If we can we can possibly prevent cancer."

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\* Handley, W. Sampson: Lymphatic Obstruction as a Factor in the Causation of Cancer, Transactions of Interstate Post Graduate Assembly, p. 117, Cleveland, 1926.

† Lymph-stasis the Precursor of Cancer. Brit. Med. Journ., October 5, 1929.

## LYMPHANGITIS IN PAPILLOMATA

Since many of the readers of this paper may not have met with my previous papers it will be necessary very briefly to restate my theory and the evidence upon which it is based. It is universally recognized that *chronic irritation* is a general, though not a universal precursor of cancer. It is necessary to use the vague word irritation because there is no specificity about the cancer-inducing irritants. They may be physical, chemical, parasitic or bacterial, and in a given area the nature of the cancer induced does not vary with the nature of the irritant employed. It has generally been thought hitherto that the irritant acts directly upon the cells which become cancerous, but no explanation or analysis of the "cancerogenic" effect has hitherto been attempted successfully. It is obviously just as likely that the effect may really be primarily an effect upon the *environment* of the future cancer cells. A study of the evidence leads directly to this conclusion, though it does not exclude the possibility of a concomitant direct irritation of the epithelial cells.

In this regard the chain of evidence is complete for one variety of cancer, namely lupus carcinoma. This is often erroneously thought to be an X-ray cancer, the result of overradiation. That this is not the case is shown by the fact that lupus cancer was fully recognized before 1895, the year in which X-rays were discovered. In a paper published in 1925\* I showed that tuberculous lupus is essentially a chronic tuberculous lymphangitis of the lymphatic system of the skin. For years the epithelium in lupus plays only a passive rôle. It may be destroyed as in ulcerative lupus, but in the non-ulcerative form of lupus it gives no particular early sign of reaction.

At the edge of an area of non-ulcerative lupus the earliest change seen is that the lymphatic vessel of each papilla is replaced by a solid cord of proliferated endothelial cells. The lymphatic can easily be recognized from its position because, as I have shown, a lymphatic vessel is the axial structure around which the papilla is built.

The blocking of this central lymphatic is followed by an increase in size of the papilla both in length, and as far as the surrounding papillæ will allow, of breadth. As the section is traced from the periphery toward the centre of the area of lupus the papillæ gradually increase in length up to five or ten times the normal. In typical warty lupus (*lupus verrucosus*) the hypertrophy of the papillæ may attain an even greater degree. The appearance of cancer upon an area of old lupus is invariably preceded by such local warty thickenings of the epithelium. Having demonstrated that proliferative lymphangitis is present beyond the apparent edge of an area of non-ulcerative lupus, and that its appearance is followed by gradual papillary hypertrophy, I considered it a fair inference that the hypertrophy was a result of the lymphatic obstruction. That inference is irresistible when one considers the pathology of elephantiasis, with its great thickening of the subcutaneous tissue and its papillary hypertrophies; undoubtedly due to lymphatic obstruction.

I have thus described the effects of obstruction of a papillary lymphatic:

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\* Handley, W. Sampson: Lupus in its Surgical Aspects. ANNALS OF SURGERY, January, 1925.

The papilla is a little physiological engine. From its blood capillaries there exudes into its connective tissue spaces a constant nutritive stream of diluted blood plasma at a certain pressure. The excess of fluid is removed and the equilibrium maintained by the drainage action of the central lymphatic. Block this lymphatic and what will happen? The first effect will be a rise in the pressure in the intercellular spaces of the papilla, and on ordinary hydraulic principles the papilla will increase in size until the intercellular pressure is equal to the pressure in the capillary blood-vessels. A second effect will be overnutrition and consequent proliferation of the papilla itself and of the overlying epithelium. But the most important effect of all for our present purpose remains to be considered. In the normal papilla a constant stream of blood fluid, along with lymphocytes, is exuding from the capillaries and passing away by the lymphatic. As soon as the lymphatic is blocked, stasis occurs and the flow of fresh blood fluid through the papilla is arrested or greatly retarded, even though just as much blood may be passing through its blood capillaries. Two consequences are inevitable: the supply of oxygen to the tissues of the papilla, to its epithelium as well as to its connective tissue, will be much reduced; furthermore, the supply of hormones to the cells of the papilla will be cut off or greatly diminished. In this connection I use the term "hormone" perhaps somewhat loosely, to signify those products of the rest of the cells of the body which are necessary to the well-being of the cells of the papilla we are considering. Here, I think, we approach the crux of the problem.

Local lymphatic stasis brings about a definite rupture of the contract in virtue of which the unicellular organism originally forswore its egotism and became a social unit. Or, in the terms of biochemistry, the epithelium covering the papilla is deprived of the supply of growth-inhibiting substance, which in a well-conducted cell community is circulated to every cell.

I have shown that local lymphatic obstruction must seriously reduce the supply of oxygen to the epithelium of the blocked papilla. It would not be surprising if, in the course of years, the affected epithelium, adapting itself to meet this difficulty, should acquire a type of metabolism in which oxygenation played a relatively subordinate part. Warburg has recently brought forward strong evidence that the carcinoma cell, as compared with the normal epithelial cell, is an anaërobe, deriving most of its energy from the hydrolysis of sugar into lactic acid, and relatively little from oxidation. This remarkable fact is in exact accord with the theory of the origin of cancer which I am presenting to you. It must not be forgotten that in dealing with such a complex matter as the origin of cancer, direct proof is, in the earlier stages, not to be expected. All that can be hoped is to fit together the isolated facts into a coherent pattern.

In remarkable accord with the view that lymph-stasis is the great general physiological factor which lays the foundations of cancer, is the flood of evidence coming from many quarters that papilloma or adenoma is the precursor of carcinoma of every variety. This is universally the case in the occupation cancers such as sweep's and paraffin cancer, in cancer due to parasites such as gongylonema (Fibiger) or bilharzia, in the experimental cancers due to tar or X-rays, and evidence is continually increasing that large clinical categories of cancer, such as cervical cancer (Bonney), breast cancer (Cheatele and Handley), rectal cancer (Mummery and Dukes) and gastric cancer (Menetrier), are preceded by papillomata or adenomata.

If, as I maintain, the papilloma or papillary adenoma is the characteristic product of local lymphatic obstruction, we are getting near to the conclusion that all carcinomas are the result of local lymphatic obstruction. The mys-

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terious action of such varied chronic irritants all producing the same final result receives for the first time an intelligible explanation. They act by setting up a local chronic obstructive lymphangitis of the part to which they are applied, which leads after a time to the production of warts, or adenomata, and after a further interval to the genesis of a carcinoma. Congenital malformation of lymphatics, seen in moles or nævi, also produces lymph-stasis, warts and sometimes carcinoma.

Such in the baldest outline is the lymph-stasis theory of cancer. In the present paper I intend to deal with only one small branch of the subject. If papillomata are the product of obstructive lymphangitis or of lymphatic mal-development it should be possible in sections of warts to demonstrate the process at work, and I wish to present the evidence that such, in fact, is the case.

*Common Warts.*—If papillomata are due to blocking of the papillary lymphatic, an infective lymphangitis is likely to be by far the most frequent



FIG. 1.— $\times 55$ . Section of a melanotic wart, or warty mole from the collection of Dr. Ernest Shaw, to demonstrate the origin of lymph-stasis and papillary hypertrophy from lymphatic malformation of congenital origin.

The papillæ are greatly hypertrophied and the epithelial layer shows cell nests, but there is no malignant change. The superficial layer of the dermis—its lymphatic zone—is occupied by a richly nucleated band of nævus cells. This band shows vertical prolongations of similar tissue occupying the axis of many of the papillæ, but not quite reaching the epithelium. It is inferred that the nævus cells are derived from irregular proliferation of the lymphatic endothelium, since a lymphatic vessel normally occupies the axis of each papilla. At one point, A, in the figure, a lymphatic vessel with an open lumen is in continuity with a solid string of nævus cells.

FIG. 2.— $\times 100$ . A highly magnified photograph of two of the papillæ from the preceding figure. Both are occupied by axial lines of nævus cells continuous with the band of nævus cells in the superficial dermis. At A the line of nævus cells possesses a distinct lumen. This lumen and the axial position of the line of nævus cells proves its origin from the papillary lymphatic by proliferation of the lymphatic endothelium.

cause of common warts. Topley and Wilson\* state that numerous workers have recorded evidence which suggests that they are infectious. Jadassohn (1896) found that they could be produced in human beings by experimental inoculation. Wile and Kingery (1921) were able to produce warts in human beings with a Berkefeld filtrate of ground-up wart material by intracutaneous inoculation. It should be noted that the successful method of infection is

\* Topley and Wilson: Principles of Bacteriology and Immunity, vol. xi, p. 1247, Arnold, 1929.

identical in principle with the accepted method for artificial injection of the skin-lymphatics.

The linear arrangement frequently seen in warts of the hand suggests that, reaching the lymphatic system at one point, the infection may travel some distance along the trunk lymphatics, coming up to the surface and causing warts along the course of the infected vessel.

Borst ("Die Lehre von der Geschwulsten") emphasizes the rôle played by irritation in the causation of papilloma, so that some of them are rightly described as inflammatory, especially the warts seen on the skin and mucous membrane in the neighborhood of chronic ulcers or scars, *c.g.*, in the larynx, and in tuberculous and syphilitic affections of the intestine. Papilloma of the bladder in aniline workers is ascribed to chemical irritation, and chronic inflammation of the bladder in gonorrhœa, stone and chronic cystitis are often associated with papillomata. That developmental conditions also play a part in causation is indicated by the occasional occurrence of congenital papilloma in the bladder, the larynx and the trachea. Parasitic infections, *c.g.*, coccidiosis of the bile-ducts, may also produce papillomata. Papillomata are likely to recur after removal.



FIG. 3.— $\times 40$ . Section of an ordinary wart of the skin showing lymphangitis. Note especially at A two proliferated papillary lymphatics uniting in a characteristic Y-shaped junction. Other papillæ, BB, also show blocked central lymphatics. The dermis beneath is occupied by a reticulum of cellular lines, exactly similar to those seen in tuberculous lymphangitis. From a specimen lent by Dr. Ernest Shaw.



FIG. 4.— $\times 100$  is a highly magnified portion of the preceding figure and shows the characteristic proliferative lymphangitis which has led to the blocking of the lymphatics of the papillæ. Note that the stalk of the Y-shaped lymphatic junction is directed away from the surface of the skin, a characteristic point of distinction from excretory ducts of the cutaneous glands.

Borst considers that a papilloma which becomes malignant is from its beginning malignant, but this line of argument is contradicted by innumerable clinical experiences of simple papillomata first showing malignancy after many years. The recurrence of papillomata is more simply explained as due to persistent residual infection of the lymph-vessels of the part.

Borst, in describing warts, refers to the appearances in the dermis as follows: "An inflammatory cell-infiltration of the papillæ and of the underlying connective tissue of the corium is present," but he gives no explanation of these appearances, nor any description of the peculiarities which indicate that the infiltration is due to a lymphangitis.

It is evident that if papilloma is due to obliterative lymphangitis some sections of warts should exhibit evidence of the process, though in others fibrotic processes might have obliterated the evidence. In order to investigate this question I asked my friend Dr. Ernest Shaw to allow me to inspect his collection of sections of warts and warty moles. In ten out of the eleven

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sections available the evidence of a proliferative lymphangitis appeared quite unmistakable. Axial lines of granulation tissue were seen in the centre of the papillæ, sometimes uniting below the papillæ in a characteristic manner, and similar branching lines of granulation tissue derived from the proliferation of lymphatic endothelium, occupied the lymphatic zone, *i.e.*, the superficial third, of the dermis.

These appearances are characteristic, but the fact will perhaps not be generally admitted until histologists have become more familiar with the lymphatic arrangements of the skin. It is a remarkable fact that I have found no reference anywhere to the occurrence of lymphangitis in connection with papillomata, but anyone who looks for the association with an open mind will find it. That cutaneous moles are localized areas of congenital lymphatic malformation is the view of von Recklinghausen and other good authorities. Figs. 1 to 4 illustrate the character of the evidence of lymphatic malformation and lymphangitis found in sections of warts.

# ERZEUGUNG VON BÖSARTIGEN TUMOREN DURCH EINSPRITZEN VON MILZBREI UND BLUT VON TUMORTRAGENDEN RATTEN UND MÄUSEN

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AUF der Konferenz der Leeuwenhoek-Vereinigung in Paris teilte *Fichera* mit, dass es ihm gelungen sei, mit Blut, Milzbrei und Organauszügen von Ratten und Mäusen, die mit Carcinom und Sarkom behaftet waren, wieder Geschwülste zu erzeugen, die histologisch den Geschwülsten glichen, die die Tiere hatten.

Durch diese Versuche sind die früheren Versuche von uns—Tumorerzeugung durch Milczrei von Tumortieren—bestätigt, ebenso unsere Versuche, mit Blut Geschwülste zu erzeugen, was kurze Zeit später auch Lipschütz und einem japanischen Forscher gelungen war.

Da in der Zwischenzeit von Woglom bei den Versuchen, an der Ratte mit Milzbrei von Tumortieren wieder Tumoren zu erzeugen, nur negative Resultate erzielt wurden, so haben wir unsere Versuche mit Milzbrei wieder aufgenommen.

Es ist uns auch neuerdings wiederholt bei Tumortieren, die keine sichtbaren Metastasen hatten, gelungen, Tumoren bei Ratten und Mäusen zu erzeugen, wenn wir Milzbrei von solchen Tumortieren nahmen, sowohl von Carcinom—wie Sarkomtieren. Nachdem diese Versuche von anderer Seite (*Teutschläder Tinozri, Fichera*) bestätigt wurden, dürfte wohl kein Zweifel mehr darüber bestehen, dass mit Milzbrei und Blut auch von Tumortieren (Ratten und Mäusen), die makroskopisch keine Metastasen enthalten, Geschwülste erzeugt werden können.

Immerhin bleibt der Einwand berechtigt, dass bei diesen makroskopisch metastasenfreien Tieren mikroskopisch schon Metastasen vorhanden sind, oder dass einzelne Krebszellen in den Organen und im Blut zirkulierten. Wenn man das Letztere annimmt, so hat die Frage nicht etwa, wie man meinen könnte, ihr Interesse verloren, da die Entstehung von Krebsgeschwülsten aus Krebszellen eine alte Erfahrungstatsache ist; sondern es würde dann sich darum handeln, warum eigentlich diese Entdeckung, dass mit dem Blut und dem Organbrei von Krebstieren Geschwülste erzeugt werden können, nicht schon längst gemacht wurde, sondern im Gegenteil dies bisher als nicht möglich galt, worauf *Fichera* in Paris besonders hinwies.

Wir haben alle Mühe, mit Geschwulstbrei Tumoren zu erzeugen, wenn wir bei der Stückchen-Impfmethode nicht genügend grosse Stücke nehmen bzw. eine genügende Menge Geschwulstbrei einspritzen. Selbst für das Rous-Sarkom hat Ernst *Fränkel* nachgewiesen, dass man nicht unter eine gewisse Anzahl von Zellen heruntergehen darf, damit das Angehen von

## ERZEUGUNG VON BÖSARTIGEN TUMOREN

Tumoren mit Zellen gelingt. Unsere Milzbrei und Blut versuche würden also, wenn man das positive Ergebniss auf wenige vorhandene Krebszellen zurückführen wollte bedeuten, dass Krebszellen in der Milz und im Blut in ganz minimaler Menge imstande sind, Krebs zu erzeugen, d.h. dass also die Krebszelle in der Zirkulation weit virulenter ist als im Tumor selbst. Ferner hätten diese Versuche gezeigt, dass, wenn wir die Tumorbildung auf das Vorhandensein von Krebszellen zurückführen, wir damit rechnen können, dass auch beim Menschen Zellen im Blute zirkulieren zu einer Zeit, wo wir klinisch nichts von Metastasen nachweisen können. Und es entsteht nunmehr die dringende Frage, ob solche Krebszellen nicht beim Menschen schon im Frühstadium in der Zirkulation vorhanden sind und ebenfalls virulenter sind als die Krebszellen im Tumor selbst.

Die Entscheidung dieser Frage ist umso brennender, als, wie wir gesehen haben, ja gerade solche zirkulierenden Krebszellen besonders fähig zur Tumorbildung zu sein scheinen. Es entstehen also auch für den Fall, dass wir nur zirkulierende Krebszellen im Blut und im Gewebe nachgewiesen haben, wo wir sie bisher nicht vermuteten, neue wichtige Probleme, die wir noch genauer erforschen müssen.

Andererseits aber sprechen unsere positiven Impfungen mit menschlicher Krebslymphe (Lymphe, Exsudat) an der Ratte gegen die Deutung, dass nur dann eine Uebertragung möglich ist, wenn Zellen im Blute sind, da es sich um Tumorzellen einer anderen Spezies handelte.

Es bleibt die Frage also offen, ob es überhaupt die Krebszelle ist, welche in diesem Falle die karzinogenen Eigenschaften ausübt, und ob nicht vielmehr ein Krebsagens, wie beim Rous-Sarkom, die tumorbildenden Eigenschaften in der Zirkulation ausübt, und dass das Auffinden einzelner Krebszellen nur ein nebensächlicher Befund ist, da diese für die Krebsbildung nicht in Frage zu kommen brauchen.

Bei unseren Arbeiten, mit Blut Tumoren zu erzeugen, haben wir uns auch mit der Frage beschäftigt, wie sich das Blut von Spontantumortieren verhält. Bekanntlich sind Spontantumoren sehr schlecht übertragbar, und wir hatten auch neulich wieder einen Spontantumor bei einer Maus an der Brust, der ebenfalls bei der Uebertragung anfangs sich bildende kleine Tumoren hervorrief, die später aber zurückgingen. Es war nun interessant, dass es mit dem Blute dieses Tieres gelang, unter 10 Tieren 2mal Tumoren zu erzeugen, die weiter wüchsen und den Tod der Tiere zur Folge hatten und transplantabel waren.

Es entstand weiter die Frage, an welche Elemente des Blutes die kanzerogenen Faktoren geknüpft sind. Wir haben schon in unserer ersten Arbeit mitgeteilt, dass es fast nie gelingt, mit dem Serum Tumoren zu bekommen. Wir nehmen jetzt das Blut aus den Axillargefässen, reiben das z.T. geronnene Blut sofort mit Kochsalzlösung an und spritzen es wieder ein. Jeder Versuch, das wirksame Prinzip von der Blutkörperchen zu isolieren, scheiterte. Es konnte immer nur dort gefunden werden, wo die Blutkörperchen waren.



Wir haben dann weiter versucht, ob es nicht möglich sei, das angenommene Krebsagens von der Krebsgeschwulst auf die Blutkörperchen zu übertragen. *Auler* hat Geschwülste mit Kochsalzlösung zu einem Brei verrieben, dann diesen stark verdünnten Geschwulstbrei scharf zentrifugiert, sodass die darüberstehende Flüssigkeit bei der Einspritzung keine Tumoren mehr gab, Setzte man nun dieser Flüssigkeit Blutkörperchen hinzu, die aus normalem Blut isoliert waren und spritzte sie Versuchstieren derselben Art, Mäusen oder Ratten, ein, so entwickelten sich dieselben Tumoren wie der Tumor, aus dem der wässerige Auszug gemacht war. Diese Resultate waren allerdings nur positiv bei dem Mäusesarkom S.37 und bei dem Rattensarkom Jensen; sie waren immer negativ bei dem Ehrlich-Carcinom und bei dem Flexner-Jobling-Carcinom.

Während dieser Versuche kam *Auler* auf die Idee, dem Jäsentumor (Rattensarkom) Blutkörperchen von einer normalen Maus hinzuzufügen und das Gemisch Mäusen einzuspritzen. Die bei den Mäusen entstandenen Tumoren konnten dreimal unter fünf erzeugten Tumoren auf Mäuse weiter übertragen werden, schon bis zur vierten Generation. Nur ganz im Anfang waren sie noch auf Ratten zurück übertragbar; wenn sie dagegen eine gewisse Grösse erreicht hatten oder von der zweiten Generation ab, konnten sie nicht mehr auf Ratten zurück übertragen werden. Auch diese Versuche gelangen nur bei dem Mäusetumor S.37 und bei dem Jensen-Sarkom, bei dem Ehrlich-Mäusecarcinom und bei dem Flexner-Jobling-Rattencarcinom gelangen diese Versuche nicht.

Die Histologie der fünf erzeugten Tumoren enthält in allen Fällen der ursprünglichen Tumorart, d.h. es wurden immer Sarkome erzeugt; in drei Fällen waren es Spindelzellensarkome, in zwei Fällen bildeten sich dagegen Tumoren, welche mehr den Charakter von Endotheliomen hatten.

## MULTIPLE MYELOMA

By WILLIAM B. COLEY, M.D.

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THE chief purpose in presenting this paper is not so much to report additional cases of a comparatively rare disease, but to try to throw some light upon the problem of treatment.

That multiple myeloma is always fatal, and that no treatment is known of any value even in checking the progress of the disease, has been so universally accepted that the question of treatment is scarcely referred to in the very considerable literature on the subject.

According to Ewing<sup>1</sup> these cases invariably have a fatal termination. But that multiple myeloma is, in most cases, highly sensitive to both the toxins of erysipelas and *Bacillus prodigiosus* and to radiation, is, I believe, definitely established. Furthermore, the inhibitory action of these two agents is not only sufficient to cause great amelioration of the symptoms—in most cases but the disappearance of the tumors, in a few cases with apparently, a lasting cure of the disease.

The most important case of our series is that of Dr. J. J. Thomas of Boston.<sup>2</sup> Although published in the *Boston Medical and Surgical Journal* in 1901, and referred to in my publication of 1913,<sup>3</sup> its real significance has never been recognized because the later history of the case has never been recorded in detail. It is a clear-cut case with the diagnosis well established by clinical and microscopical evidence. What makes it unique is the later history. At the time of Thomas' report, only a few months had elapsed since the operation and the appearance of rapidly developing metastases to the ribs. It was stated that the patient was taking Coley's toxins, and had shown improvement. As a matter of fact, the improvement continued. The toxin treatment was kept up, twice a week, for two years, under my direction. The patient made a complete recovery, and remained well for five years when he died of acute lobar pneumonia.

So far as is known, this is the only case on record of a multiple myeloma that has recovered under any form of treatment, and the patient remained alive for five years, except the Gilmore case in which there was a difference of opinion in regard to the diagnosis.

The Marine Hospital case of multiple metastatic myelosarcoma with extensive involvement of the bones and soft parts, reported by Christian and Palmer<sup>4</sup> is, in my opinion, a case of probable multiple myeloma primary in the tibia (see Case XIV). The microscopical diagnosis of Dr. Ewing Taylor was that of myelosarcoma concurred in by Doctors Ewing and Codman. Amputation at the thigh was performed in September, 1925. Three months later extensive multiple metastases developed in the stump, inguinal glands, clavicles, skull, abdominal wall and elsewhere. All disappeared under prolonged toxin treatment, without radiation or other treatment; the patient regained his lost weight of forty pounds and has remained in good health without evidence of a recurrence, up to the present time, more than four and one-half years since the beginning of treatment.\*

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\* Doctor Wood states that microscopically it is a metastatic carcinoma. Diagnosis of multiple myeloma was made by Doctor McWhorter.

As further evidence of the inhibitory action of the toxins combined with irradiation, I might cite the case of Mrs. C. (see Case V) which is briefly as follows:

A female, aged forty-four years, was brought to the Memorial Hospital in November, 1928, from a home for incurables, after her condition had been pronounced hopeless by Dr. Howard Lilienthal. On examination I found a large tumor involving the upper third of the femur, with a pathological fracture; the disease invaded the sacrum; there was



FIG. 1.—Case V. Plasma-cell myeloma of femur and spine.

paraplegia, and considerable loss of weight. I agreed with Doctor Lilienthal that the condition was hopeless. At the urgent request of the patient's husband I consented to give her a brief course of toxin treatment and irradiation. The toxins alone were used at first, with marked improvement; at the end of three weeks, one radium pack was applied, with rapid and continuous improvement. In this case the original diagnosis of Doctor Ewing was that of endothelial myeloma, and the case was reported as such by Coley and Coley.<sup>6</sup> On reviewing the sections, recently, Doctor Ewing and Doctor Stewart, of the Memorial Hospital laboratory, have concluded that the case should be

## MULTIPLE MYELOMA

classified as a plasma-cell myeloma. (Fig. 2.) No radiation had been applied to the spinal tumor, this tumor apparently disappearing under toxins alone as the patient completely recovered from the paraplegia and had no return of it up to the time of her death, two years later, from metastases to the brain. I think there is every reason for believing that the result in this case might have been different had the toxin treatment been kept up for a longer period of time instead of being discontinued at the end of five months.

In another case of plasma-cell myeloma, an apparent recovery has followed the use of irradiation when applied at the Memorial Hospital under the direction of Doctor Stone and Doctor Herendeen.

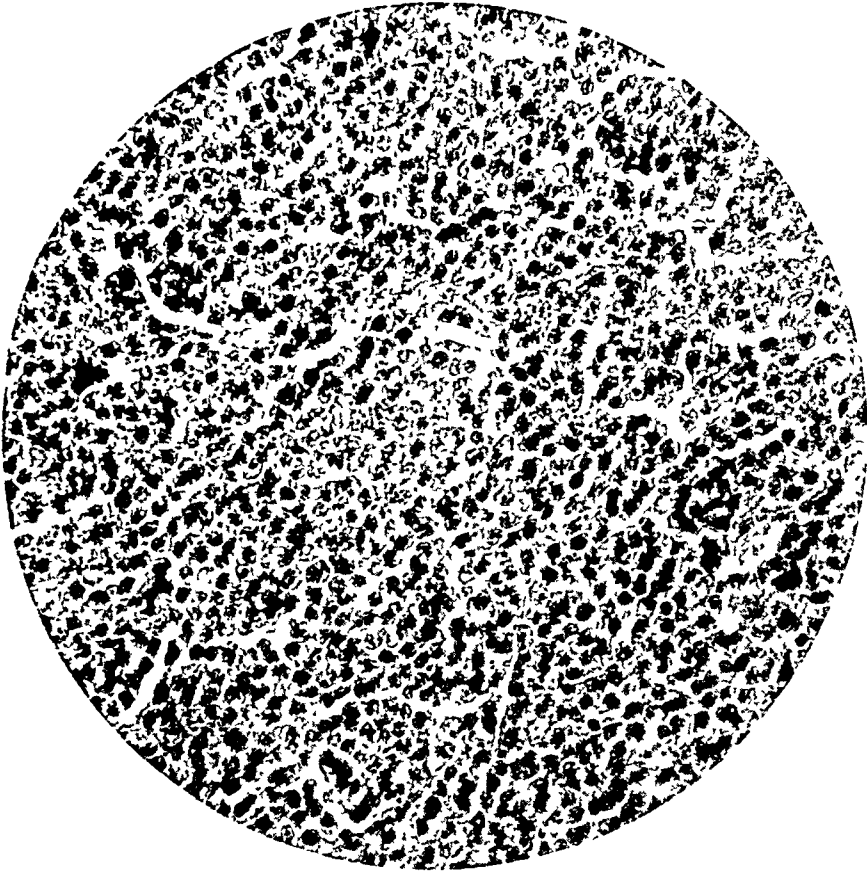


FIG. 2.—Case V. Plasma-cell myeloma.

L. C., female, aged fifty-two years, was admitted to the Memorial Hospital in August, 1926, with a history of having had shooting pains in her right leg for nearly three years. A röntgenographic diagnosis of osteitis fibrosa cystica, or giant-cell sarcoma, had been made. A biopsy was performed, revealing a tumor, the structure of which was typical of plasma-cell myeloma. Under irradiation at the Memorial Hospital she showed remarkable improvement, with almost complete restoration of function. When last heard from, more than three years later, she was able to get about comfortably, and was, apparently, free from all evidence of the disease.

In another case, beginning as a solitary plasma-cell myeloma, the disease was almost completely controlled by radium-pack treatment, the patient remaining well for two years (see Case VI).

J. K., male, aged fifty-eight years, whose first symptoms, pain and soreness around the greater trochanter, appeared in December, 1923. Numerous diagnoses were made from the clinical and röntgenographic evidence. Biopsy revealed a typical plasma-cell

myeloma. There was a pathological fracture. The radium pack was applied by Doctor Stone, over three different areas. The patient remained well for two years when he developed multiple metastases; the disease progressed rapidly, causing death in a short time.

Here, again, there can be no question of the value of irradiation in a case of definitely proven multiple myeloma. I believe if this treatment had been continued, supplemented by systemic toxins, it is not improbable that the disease might have been held under control for a longer period of time, possibly permanently.

*Frequency.*—Multiple myeloma is a very rare disease. When Thomas reported his case before the American Neurological Association in 1901, he was able to find only nineteen cases in medical literature. In 1920 there were only 118 cases on record. The number has increased more rapidly in recent years, owing, in part, to the steadily growing interest in the study of bone tumors. Geschickter and Copeland, in their publication of 1928, in addition to describing the thirteen cases observed at the Johns Hopkins Hospital since it was founded, called attention to 425 additional cases that they had been able to find in the medical literature up to 1927, and they have included in their paper a most valuable bibliography, giving the reference to these cases in the order of publication.

*Onset.*—Multiple myeloma, in most cases begins with a fairly characteristic onset, without any known predisposing cause unless it be local trauma, which has been observed in about 20 per cent. of the cases. The patient complains of severe localized pain. The pain is usually intermittent in character, greatly aggravated by motion, and disappearing when the body or limb is at complete rest. This pain continues to increase in severity and is usually treated for neuritis of one of the long bones, for lumbago, or for rheumatism if in the spine. Loss of weight and anæmia often follow quickly.

*Clinical Appearance.*—Multiple myeloma has certain very definite clinical characteristics which enable one to make a diagnosis in the majority of cases. These characteristics may be described as follows:

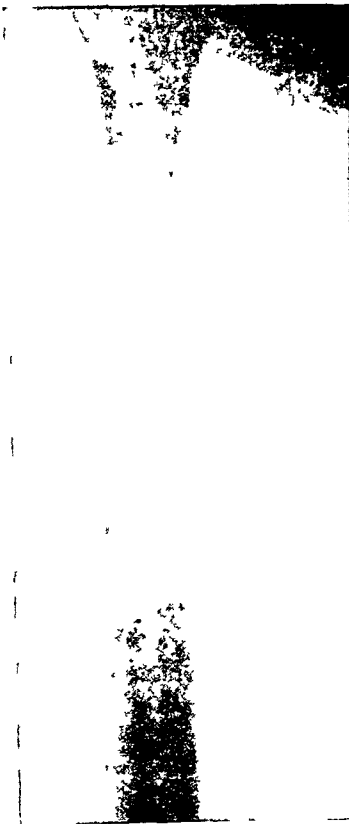


FIG. 3.—Solitary plasma cell myeloma before treatment

1. *Tumor.*—A tumor originating in the cancellous portion or in the marrow of a bone.

2. *Site.*—Multiple myeloma has a predilection for certain bones, and the bones most often affected in the early stages of the disease are: the ribs, spine, humerus, femur, knee and pelvis. In our own series the disease was first noticed in the following bones: humerus, 2;

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femur, 4; tibia, 2; spine and ribs, 3; ribs, 1; ribs and skull, 1; ilium and tibia, 1; clavicle and ribs, 1.

In three cases a diagnosis of solitary plasma-cell myeloma was made.

3. *Multiple Involvement*.—While this may not be observed in the early stages of the disease, multiple foci are soon discovered which may have existed from the very beginning.
4. *Pathological Fracture*.—The lesions are characterized by bone destruction with a complete absence of new bone formation. This destructive process proceeds rapidly so that in many instances a pathological fracture may occur within two or three weeks of the first symptom (localized pain).

In our own series, a pathological fracture was observed in 50 per cent. of the cases. This is slightly higher than has been found in any other form of bone neoplasm.<sup>6</sup> In the Johns Hopkins series, a pathological fracture was noted in 62 per cent. of the cases.

5. *Paraplegia*.—Early paraplegia occurs in cases in which the spine is involved. In these cases we may find a distinct kyphosis (observed in two of our cases). There may be varying stages of scoliosis or lordosis, and even a marked shortening of the spine due to disintegration and collapse of the vertebra. Paraplegia was noticed in 40 per cent. of our own series. The disease develops very slowly. It is characterized first by weakness in the legs, increasing difficulty in urinating, Babinski's sign, and finally, definite paraplegia.
6. *Bence-Jones Bodies*.—The presence of Bence-Jones bodies has been observed in about 8 per cent. of all cases. While this condition may be associated with other diseases, it is of great diagnostic significance in multiple myeloma, especially in the presence of multiple lesions of bone with the clinical and röntgenographic features of multiple myeloma.
7. *Nephritis*.—While changes in the kidney were noticed in 70 per cent. of the Johns Hopkins series, chronic nephritis has not, by any means, been constant in our own series.
8. *Backache*.—Severe backache is always present in cases in which the spine is involved, but in other cases localized pain, greatly exaggerated by muscular strain, is the first symptom.

*Röntgenographic Appearance*.—The röntgen-ray will usually reveal features which, while not absolutely pathognomonic, still point strongly to a diagnosis of multiple myeloma. These features include sharply localized areas of bone destruction in a number of different bones. They often have a "punched out" appearance. If the ribs are involved, there may be a large number of areas of destruction giving a distinct mottled appearance. The bones most frequently affected are the ribs, the spine, the skull, and, less often, the long bones.

If the disease starts in one of the long bones, first as a solitary lesion, a plasma-cell myeloma, the röntgenogram may closely resemble that of an endothelial myeloma. This resemblance applies to the microscopic picture as well.

*Clinical Course.*—The clinical course depends much upon the locality of the disease, in other words, upon the bones affected. The solitary plasma-cell myeloma which, in some cases, especially those of the humerus, closely resembles a cyst or a giant-cell tumor, cannot be differentiated from an endothelial myeloma. In these cases, early pathological fracture is the rule. According to Geschickter and Copeland, 60 per cent. show a thoracic deformity, often being mistaken for Paget's disease or osteitis fibrosa cystica generalized. In thoracic involvement, the region on either side of the sternum and the clavicles are favorite sites. While the tumors may be palpable, they are nearly always small and only slightly raised above the normal surface of the bone. The tumors of the ribs and skull are soft and resilient and so highly vascular that pulsation often is easily detected.

A brief analysis of the following four series is of interest.

*Meyerding's*<sup>7</sup> Series of thirteen cases treated at the Mayo Clinic: males, 9; females, 3; sex not stated, 1. Ages ranged from forty-three to sixty-nine years. Duration of disease extended from three months to four years. Microscopical examination made in 4 cases. Trauma noted in 4 cases (indefinite in 1 case). Locality of disease: skull, 4; ribs, 5; humerus, 2; spine, 4; femur, 2.

*Thomas's*<sup>8</sup> Series of eighteen cases collected in 1901: males, 12; females, 4; sex not stated, 2. Ages ranged from thirty-six to eighty years. Duration of disease extended from two months to seven years. Microscopical examination made in 13 cases. Locality of disease: ribs, 11; spine, 6; humerus, 2; skull, 3; clavicle, 2.

*Geschickter and Copeland's* Series of thirteen cases observed at the Johns Hopkins Hospital: males, 9; females, 4. Ages ranged from thirty-seven to seventy-two years. Microscopical examination made in 11 cases.

*Personal* Series of sixteen cases: males, 12; females, 4. Ages ranged from sixteen to sixty-eight years. Microscopical examination made in 11 cases. Trauma noted in 7 cases.

Thomas found the presence of albumose in the urine in eleven of the nineteen cases of undoubted myeloma. He states that while this is by no means constant, it is certainly present in more than traces in a majority of the cases, and its presence is always enough to direct our attention to the possibility of disease of the bones, and may lead to a correct diagnosis.

*Etiology.*—In regard to the etiology of multiple myeloma we know just as little about it as we do about that of malignant tumors in general. Like carcinoma it is found chiefly in middle life. Eighty per cent. of the cases thus far observed have occurred between the ages of forty and seventy years. Geschickter and Copeland state that only 5 cases were found under the age of thirty-five years, and in two of these the diagnosis rested on clinical and röntgenographic evidence. One of our cases occurred in a youth aged seven-

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teen years, and Gillespie, of Fort Worth, Texas, has reported a case in a child aged eighteen months.

The finding of early multiple foci of disease in widely separate bones suggests the possibility or probability that we are dealing with a constitutional disease in which the causative agent is present in the circulation and finds a foothold in the marrow of certain bones where, by reason of impaired circulation or local trauma, it finds a favorable site for development.

Multiple myeloma resembles endothelial myeloma or Ewing's sarcoma so closely that it cannot always be differentiated by the clinical and röntgenographic evidence; and in a few cases the microscopic picture of the two conditions has been found to be strikingly similar. The age incidence, however, is somewhat different, endothelial myeloma occurring frequently in childhood or youth, whereas multiple myeloma is seldom found under the age of forty years.

These two conditions, we believe, furnish strong evidence in support of an extrinsic or infectious origin, and the occasional marked rise in temperature further supports this view. While some writers would explain this rise of temperature as being due to intercurrent infections, we believe it more probably due to degeneration and necrosis of certain areas of very rapidly growing tumors of bone, with the consequent absorption of the products of degeneration. We have observed a case of very rapidly growing tumor of the upper end of the humerus in a boy aged five years, which, in spite of heavy Röntgen therapy, grew to the size of his head within three months. A diagnosis of endothelial myeloma was made. In this case the temperature would rise for a week at a time to  $103^{\circ}$  or  $104^{\circ}$  daily, and would then subside, later rising. There was never any evidence of infection in this case. In one of our most recent cases of multiple myeloma (ilium, femur and tibia) in a young man aged seventeen years, in which the disease developed very rapidly, the temperature rose to  $103^{\circ}$  or  $104^{\circ}$  daily for weeks. The whole course of the disease was a little over three months.

If we accept the theory that all types of sarcoma, including endothelial myeloma and multiple myeloma, are due to some unknown extrinsic agent or virus, then the close similarity of these cases to osteomyelitis or inflammatory condition of bone is easily explained, and the problem then would be to differentiate two groups of tumors, *i.e.*, (1) those tumors that are now regarded as inflammatory, due to certain known micro-organisms or infectious agents; and (2) those due to some infectious agent which, up to the present time, has never been discovered or definitely classified. Until we have further knowledge, there is little to be gained by a further discussion of the etiology.

*Gross Anatomy.*—This has been best described by Ewing in his textbook on "Neoplastic Diseases" (1928). To quote him:

"The tumors are soft or firm, translucent or opaque, and whitish, gray, or deep red according to vascularity. Hæmorrhage, infarction, blood cysts, and necrotic areas may be present. The bone tissue suffers active absorption and the shafts become very thin,



or multiple perforations result, or fractures occur. After passing the periosteum the surrounding tissues are diffusely invaded.

"Many cases terminate without metastases in the organs, but distant secondary growths have been found in the liver, spleen, kidney, lung, and ovary, while in certain very malignant cases, that probably belong in this category, nearly every organ in the body may be involved."

"While in some cases the cells of myeloma exhibit the features of plasma-cells, large or small with a single or multiple nuclei, yet in the entire scope of tumors which prob-



FIG. 4.—Case VII. Solitary plasma-cell myeloma of femur.

ably belong in this class the cells vary widely in size and character. In some cases the entire tumor is composed of loosely packed typical plasma-cells, 8 to 12 in diameter, round, oval, or polygonal, and with opaque, amphophile, non-granular cytoplasm. The single or multiple nuclei are relatively small, eccentric, or protruding from the cytoplasm, surrounded by a clear zone, and presenting blocks of chromatin arranged along the nuclear membrane. Mitotic figures are observed in many cases, but are less numerous when the cells are typical plasma-cells. Certain cytoplasmic bodies have been interpreted as centrosomes (Christian). The clear zone about the nucleus has been described as a vacuolated secretory product. In rare cases the round cells are mingled with spindle cells which probably result from pressure (Wieland).

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"In a second group of cases the cells are larger, giant cells with multilobed nuclei appear, multiple and vesicular nuclei are more prominent, nucleoli are large and acidophile, the resemblance to plasma-cells is not striking, the tumors are more malignant and metastases occur. Here one finds a structure which recalls lymphosarcoma with large cells. . . .

"Bone trabeculae undergo simple absorption, or, in the case of compact bone, osteoblasts are found in lacunae. The tumor never produces bone. An inflammatory reaction with exudate of lymphocytes and plasma-cells may mark the advance in bone marrow, periosteum, or other tissue."

*Histogenesis.*—"That the tumor cells in one group of cases represent various forms of plasma-cells," states Ewing, "is strongly attested by the comparison made by Christian. In one group of cases the identity with plasma-cells is so striking as to suggest that those writers who doubt this identity have never seen such a case.

"In another group of cases the cells lack close resemblance to plasma-cells, and their form and arrangement strongly suggest an origin from the blood-forming cells of the marrow.

"Thus if one classes myeloma according to the views of different observers concerning the origin of the tumor-cells, the following groups appear: (1) Plasmocytoma, (2) erythroblastoma, (3) myelocytoma, adult and embryonal, (4) lymphocytoma. Whether such varied interests are actually represented in the scope of multiple myeloma, or whether we have to deal varying grades of anaplasia in a single cell of origin remains to be determined. At present the data seem to favor the former alternative."

Recent writers, especially Geschickter and Copeland, do not attempt to distinguish between the many different varieties based upon the morphogenous characteristics, but include them all in two groups, *i.e.*, (1) plasma-cell and (2) myelocytic type, and they claim that it is not always possible to differentiate these two. They have repeatedly observed cases in which authorities who have examined the same sections have differed between the two terms.

*Differential Diagnosis.*—The clinical features of multiple myeloma have already been described. The condition most likely to simulate it is endothelial myeloma. In both conditions the disease, if not multiple when first observed, soon shows multiple lesions. In both, the trouble starts in the marrow of the bone and destroys the adjacent bone. In multiple myeloma this destructive process is less widespread, seldom involving any great length of the shaft of a long bone, but confining itself to a limited area of bone-destruction, and causing an early pathological fracture. This condition is much more highly vascular and often shows distinct pulsation. In the ribs, early fracture gives rise to crepitus on palpation, and marked pain on deep inspiration or movement of the ribs.

While the röntgenogram of multiple myeloma (solitary type) of a long bone may resemble closely that of a giant-cell tumor, the location usually is quite different. The giant-cell tumor in most cases is found near the epiphysis of the bone while the multiple myeloma is in the shaft.

Then, again, the course of the disease is much more rapid in multiple myeloma and pathological fracture occurs more quickly. Furthermore, the pain in multiple myeloma is much more severe.

Another condition that may be mistaken for multiple myeloma is metasta-

tic carcinoma. The röntgenogram may simulate a multiple myeloma so closely that it is impossible to differentiate it, and the diagnosis may not be possible until a microscopic section has been examined or an autopsy performed. Two years ago there was such a case observed at the Memorial Hospital.

*Solitary Plasma-cell Myeloma.*—Only one example of solitary plasma-cell myeloma was found in the first thousand cases of bone sarcoma recorded in the Bone Sarcoma Registry. We have had two examples of this type of myeloma at the Memorial Hospital during the last four years. One occurred in a male aged forty-eight years, and the other in a female aged fifty-two years. In one the disease originated in the mid-shaft of the humerus, and in the other, in the upper end of the femur. In the humerus case the disease at first showed signs of regression, but a pathological fracture developed which showed no tendency to unite in spite of heavy radiation and toxin treatment. Amputation was performed, and the patient is well at present, about six months later. The femur case responded well to radiation, and the patient is in good health at the present time, more than three years later.

*Metastatic Carcinoma.*—In making a differential diagnosis between multiple myeloma and metastatic carcinoma one should bear in mind that Bence-Jones protein is rarely found in metastatic carcinoma, and that while the two conditions are apt to occur in similar bones, multiple myeloma usually involves the flat bones while metastatic carcinoma, particularly the breast cases, is more often found in the long bones, especially in the femur. A carcinoma of the prostate most frequently metastasizes to the bones of the pelvis or the lower spine. Then again, the multiplicity of lesions is usually a much more prominent feature in multiple myeloma than in metastatic carcinoma. The röntgenographic appearances of the tumor may be of help in making a diagnosis: In metastatic carcinoma of the prostate, there is a certain amount of bone production while in multiple myeloma the process is always one of bone destruction.

*Fibrocystic Disease.*—This condition may in certain cases resemble multiple myeloma, but the locality of the tumor should render the diagnosis comparatively easy. Fibrocystic disease is most frequently found in the long bones while multiple myeloma is found chiefly in the flat bones.

The greatest difficulty will be encountered in making a diagnosis between solitary plasma-cell myeloma, metastatic carcinoma and giant-cell tumor. However, in cases of doubt, the clinical history, the multiplicity of lesions, the bones involved, and the presence or absence of Bence-Jones Bodies, will be of a great diagnostic value.

*Metastases.*—Most writers have stated that multiple myeloma never metastasizes in the lymph-glands or in the viscera, but is found only in bones, preferably the flat bones. While this is true in a general way, there have been a number of cases reported in which visceral metastases have been observed.

In a paper on "The Multiple Myelomata and Their Ability to Metasta-

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size,"<sup>9</sup> Symmers reports two cases from the Pathological Department of Bellevue Hospital. It is worthy of note that since the establishment of the Pathological Laboratories of Bellevue Hospital twelve years previously, only eight cases of multiple myeloma were encountered in 6000 autopsies.

Symmers believes that in embryonal life "the liver and spleen are hæmopoietic organs auxiliary to the bone-marrow, but in extra-uterine life the marrow assumes the task of hæmatogenesis to the exclusion of the liver and spleen." Under certain conditions, he states, it may be possible for this blood-forming function of the liver and spleen, which was lost at birth, to be reawakened. He regards his second case, as one reported by Christian, in which there were secondary neoplastic nodules in the soft parts of the arm and axilla, as representing the only really indisputable examples of genuine metastatic myelomata to be recorded. Both of them effectually violate the generally accepted dictum that the myelomata do not metastasize by cell transplantation.

*Multiple Myeloma in Early Life.*—Nearly all writers state that multiple myeloma is never found under the age of thirty years, and this statement is subscribed to by Geschickter and Copeland in their recent paper on the subject. Our own series contains one case of rapidly progressing disease in a boy aged seventeen years, and Gilmore,<sup>10</sup> of Fort Worth, Texas, reports a case occurring in a child aged eighteen months when the first symptom appeared. Because of the extreme youth of the patient, this case has not been accepted by some pathologists as a true multiple myeloma.

While in this case six pathologists of the Bone Sarcoma Registry committee each gave a different diagnosis, in the opinion of Dr. Francis Carter Wood it was a multiple myeloma. The clinical history of destructive lesions of many bones, the extreme sensitivity to radiation, the Bence-Jones protein in the urine, all point strongly to a diagnosis of multiple myeloma. If this case, strictly speaking, does not belong to this group, it certainly comes under that of endothelial myeloma or Ewing's sarcoma with very wide generalization, and becomes the first case on record of an endothelioma with wide generalization that has been cured by radiation alone, and the patient well for five years.

### SUMMARY OF RESULTS OF TREATMENT IN THE CASES WHICH FORM THE BASIS OF THE PRESENT REPORT

There were three cases treated with the mixed toxins of erysipelas and *Bacillus prodigiosus* alone, *i.e.*:

CASE I.—(Doctor Thomas' case.) The disease involved the spine and ribs after incomplete operation on the spine. The patient recovered, and remained well for five years, when he died of pneumonia.

CASE XIV.—(Marine Hospital case.) After amputation of the tibia in September, 1925, multiple metastases developed in skull, clavicle, femur and soft parts. The patient made a complete recovery and regained forty pounds of lost weight. He is in excellent health at the present time, with no evidence of a recurrence four and one half years later.

CASE XII.—Was treated with toxins for a few weeks, with little apparent effect. The patient lived out of town and the treatment was not pushed to the point of producing severe reactions. New lesions developed rapidly in the ribs and spine, and treatment was abandoned.

There were eight cases treated by toxins and radiation, as follows:

CASE V.—Involving the femur and spine (paraplegia and pathological fracture of femur when the treatment was begun). (Figs. 1 and 2.) One radium-pack treatment was given to the femur; none to the spine. The toxins were kept up for four to five months. The patient made a complete recovery; the paraplegia disappeared and the fracture united. She remained well for two years and then died of metastasis to the brain.

CASE IX.—Plasma-cell myeloma, solitary, of the humerus treated with radiation and toxins. There was little change in the size of the tumor. A pathological fracture occurred and showed no tendency to unite. Amputation was performed, followed by further toxin treatment. The patient is well six months later.

CASE III.—Involving the spine and ribs. Treated by toxins and Röntgen-ray with marked temporary improvement. After six months it was impossible to hold the disease in check and the patient died shortly afterwards.

CASE XI.—Involving the ribs and skull; treated with toxins and radium. Marked improvement has been noticed. The toxin treatment has been continued at home and the patient is able to carry on his occupation. This is a recent case.

CASE XIII.—(Treated by Doctor Bloodgood.) Involving the femur, with pathological fracture. Under eighteen doses of toxins marked improvement was noticed with reunion of fracture. The bone was refractured from walking too soon without proper support. Patient is now taking Röntgen-ray therapy. The bone is again reuniting, and there is little, if any, evidence of the disease remaining. This is a recent case.

CASE X.—Involving the humerus; pathological fracture. Under toxins and radium the bone united. Three months later another lesion developed in the clavicle; another fracture. Recovery under treatment. Three months later the disease recurred in two ribs. This disappeared under similar treatment. Three months later the other humerus became involved; recovery under treatment. Three months later the dorsal spine became involved; recovery under treatment. Fifteen months later a lesion appeared in the cervical spine. Died June, 1930.

CASE VIII.—Involving the spine and ribs. The disease was held under control for four years by Röntgen-ray; it later metastasized to two ribs; was not controlled by further radiation; greatly steadily. The patient developed complete paraplegia with paralysis of the vocal cord; had lost fifty-six pounds in weight, and was confined to bed when the toxin treatment was begun (August, 1928). A complete recovery took place (with exception of bladder of which he lost control in 1924 at the time of the original operation) and he is in good health with no evidence of disease, nearly two years and four months later.

There were four cases treated by radiation alone, as follows:

CASE VI.—Involving the femur. The patient remained well for two years and then developed multiple metastases causing death in a few months.

CASE XVI.—Involving the clavicle. Excision followed by radiation. Temporary improvement; death in one and a half years.

CASE XV.—Involving the tibia. Marked improvement under radiation. Disease held in check for one year.

CASE VII.—Involving the femur (solitary). (Fig. 4.) Complete control under Röntgen therapy. Patient well more than three years later.

In two other cases, II and IV, the disease was so far advanced that, while toxins were given for a very short period, nothing was to be hoped

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for by treatment; nearly every bone was involved. In a recent case, primary in the ilium, in a young man aged seventeen years, the patient had been taking small doses of toxins for about two weeks in conjunction with Röntgen therapy. He was running a temperature of 104° daily and was profoundly ill. Röntgenograms showed both femurs and tibiae to be involved. Death occurred in about three months.

We believe that the results obtained in this series fully justify our opinion that the prognosis in multiple myeloma is not always fatal; and that if the method of treatment herein described is employed (toxins of erysipelas and *B. prodigiosus* combined with irradiation) marked improvement with control of the intense pain may be looked for in most cases. In a certain number, complete control of the disease and a permanent cure may be effected.

### CONCLUSIONS

1. The prognosis in multiple myeloma is by no means so hopeless as is universally believed.

2. Most cases of multiple myeloma of both the ordinary and the solitary varieties are extremely sensitive to both the toxins of erysipelas and *B. prodigiosus* and to radiation.

3. In a number of cases the disease has been held in check for a very considerable period of time by the toxins alone or radiation alone, or by a combination of both agents.

4. In four cases, two treated by toxins alone, one by toxins and radiation, and one by radiation alone, respectively, the disease has apparently been eradicated, and the patient has remained well for a sufficient length of time to justify the hope of a permanent cure.

5. No case of multiple myeloma should be given up as hopeless without a prolonged trial of both toxins and radiation.

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# LA MÉTAPLASIE ÉPITHÉLIALE ET SES RAPPORTS AVEC LES TUMEURS

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L'EXISTENCE de tumeurs hétérotopiques telles que les épithéliomas malpighiens dans le domaine des muqueuses cylindriques est connue depuis fort longtemps. L'interprétation de ces faits a suscité de nombreuses discussions; les hypothèses multiples émises à ce sujet se ramènent essentiellement aux deux suivantes: l'une admet une malformation embryonnaire, l'autre, une métaplasie malpighienne de la muqueuse cylindrique.

Or, depuis que la possibilité d'une telle métaplasie a été indiscutablement démontrée, la deuxième hypothèse a nettement gagné du terrain, et, puisque la métaplasie, elle-même, semble conditionnée par des processus inflammatoires chroniques on n'a pas manqué d'insister sur les relations très étroites qui se révèlent ainsi entre les processus irritatifs chroniques, la métaplasie et les tumeurs. Les adeptes de la théorie irritative du cancer ont donc tiré de la métaplasie un argument apparemment très démonstratif en faveur de leur conception; Ménétrier par exemple affirme que "l'intérêt de ces faits est considérable au point de vue de la pathogénie du cancer puisque toutes ces modifications de l'épithélium sont suscitées par des irritations, des inflammations chroniques qui se montrent ainsi génératrices du processus cancéreux."

Mais en étudiant de plus près les rapports qui existent entre l'irritation chronique et la métaplasie d'une part, entre la métaplasie et les tumeurs hétérotopiques d'autre part, on ne manque pas de constater des faits troublants et peu favorables à la conception que nous venons de rappeler. Ce sont ces faits que nous voudrions brièvement exposer ici.

Voyons d'abord dans quelles circonstances et dans quelles régions s'observe la métaplasie malpighienne des muqueuses cylindriques. Pour répondre à cette question, il ne faut envisager que les cas où la métaplasie apparaît réellement démontrée. Or, il est évident que la présence d'un îlot malpighien parfaitement circonscrit au milieu d'une muqueuse cylindrique n'est pas une preuve d'un processus métaplasique, il peut tout aussi bien s'agir d'une malformation embryonnaire. Nous admettons par contre l'existence d'un processus métaplasique lorsque l'apparition du tissu malpighien s'observe avec une certaine fréquence dans des conditions étiologiques identiques et surtout lorsque la présence de formes intermédiaires permet en quelque sorte de suivre l'évolution du changement structural. Encore faut-il que, dans tous ces cas, l'on puisse exclure, pour des raisons topographiques, l'immigration d'un épithélium malpighien de voisinage.

Ces phénomènes métaplasiques, indiscutables à notre avis, s'observent avec une grande fréquence dans tout le domaine des voies respiratoires. La transformation malpighienne du revêtement bronchique apparaît avec une

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rapidité parfois surprenante dans les processus inflammatoires subaigus et chroniques même chez l'enfant. L'épithélium bronchique, pourrait-on dire, a une tendance manifeste à devenir malpighien.

Au niveau du corps thyroïde la métaplasie malpighienne du revêtement acineux est plus rare, mais des recherches attentives permettent néanmoins de constater ce processus dans bien des thyroïdites chroniques. On observe alors la stratification de l'épithélium, la formation de bourgeons saillants à l'intérieur des vésicules dont les éléments cellulaires, de forme polygonale, sont, reliés entre eux par des filaments d'union.

Dans le domaine du tube digestif, la métaplasie malpighienne est presque propre aux glandes salivaires et au pancréas. En ce qui concerne les glandes salivaires, le fait est classique; il suffit de pratiquer la ligature du canal

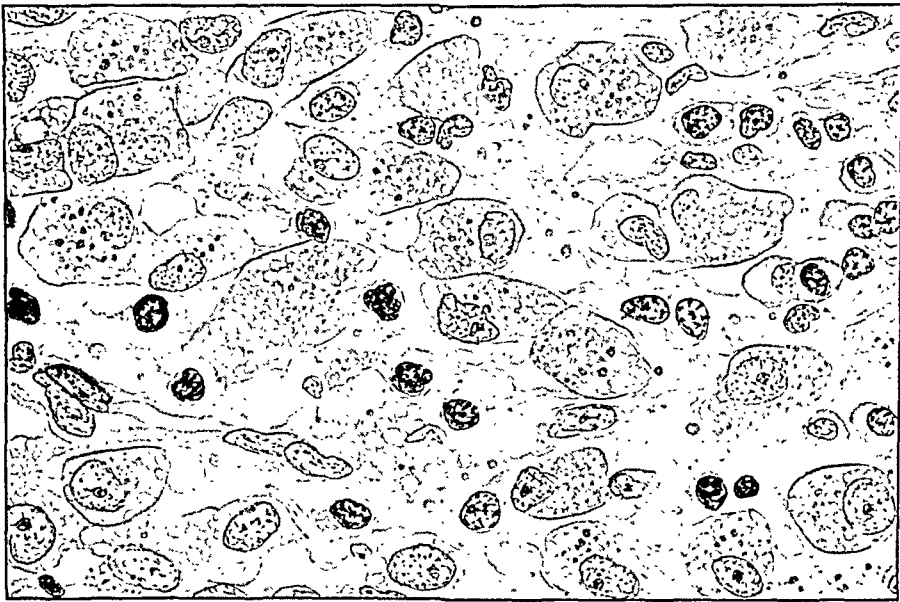


FIG. 1.—Îlot gastrique de l'œsophage au voisinage d'un épithélioma du type gastrique (à gauche).

excréteur ou d'injecter dans le système canaliculaire une substance irritante (goudron, huile de scharlach, etc. . . .) pour provoquer, à coup sûr, une transformation malpighienne de l'épithélium canaliculaire.

Dans le pancréas, l'un de nous a démontré que l'apparition de bourgeons malpighiens dans les canaux excréteurs est très fréquente dans les pancréatites chroniques.

Parmi les autres muqueuses, qui sont plus fréquemment le siège de métaplasies malpighiennes, il faut encore citer l'épididyme. Des recherches systématiques montrent que l'épithélium cylindrique de cet organe prend assez souvent des caractères malpighiens aussi bien dans les épididymites subaigues gonococciques que dans les épididymites tuberculeuses.

Au niveau du corps utérin, la fréquence de la métaplasie malpighienne, en dehors des tumeurs, a été l'objet de nombreuses discussions, mais nous considérons avec Kaufmann et beaucoup d'autres auteurs que ce fait est très rare.

Mentionnons encore que dans la glande mammaire la métaplasie malpighienne des conduits galactophores a été observée à différentes reprises et



provoquée expérimentalement par injection d'huile de scharlach (Fischer).

Quelles sont maintenant les conclusions que l'on peut tirer de ces faits d'observation?

En ce qui concerne le mécanisme même de la métaplasie épithéliale, le fait est aujourd'hui reconnu par tout le monde qu'il n'y a pas transformation structurale de cellules adultes; ce sont les cellules jeunes en voie de prolifération qui, en se différenciant, changent d'orientation et prennent un caractère différent de leur cellule-mère; la métaplasie est, suivant la formule de Lubarsch, une *régénération atypique*.

D'autre part, nous avons vu que la métaplasie malpighienne ne s'observe que dans des régions déterminées et ce fait montre nettement, à notre avis, que l'irritation chronique ne résume pas toute la pathogénie du processus. Si



FIG. 2.—Aspect de la tumeur à un fort grossissement. On voit des cellules isolées remplies de mucus.

réellement la métaplasie était la conséquence directe d'un facteur irritatif exogène, non spécifique, elle devrait se réaliser beaucoup plus souvent et dans n'importe quel endroit. Or, on connaît des muqueuses telles que celle de l'estomac ou de l'appendice où les processus inflammatoires chroniques sont d'une extrême fréquence et où la métaplasie malpighienne n'a jamais été observée au moins chez l'homme. L'influence d'un facteur local semble donc indéniable et ce rôle du "terrain" que nous retrouvons avec toute son importance dans la pathogénie du cancer s'affirme encore davantage lorsqu'on étudie de plus près l'évolution du processus métaplasique.

On se rend alors compte que dans le domaine d'une muqueuse irritée où

les mêmes conditions semblent réalisées sur une large étendue, la métaplasie n'est pas d'emblée diffuse—les éléments malpighiens apparaissent par îlots et ce n'est que plus tard que ces îlots s'étendent, gagnent la muqueuse environnante et arrivent finalement à la confluence. L'analogie de ce processus avec l'éclosion du cancer après goudronnage est frappante.

En invoquant donc l'irritation chronique comme facteur étiologique de la métaplasie, on n'explique rien. Tout indique l'intervention de facteurs très spéciaux qui ne se réalisent que dans des conditions déterminées; et ces facteurs, il faut l'avouer, nous les ignorons totalement.

Les mêmes difficultés se présentent, lorsqu'on cherche à préciser les rapports entre la métaplasie et les tumeurs hétérotopiques.

Pour les adeptes de la théorie irritative, les faits sont très simples: l'irritation crée la métaplasie et la métaplasie fournit le terrain sur lequel se développe la tumeur. La métaplasie prend ainsi la signification d'une *lésion précancéreuse*. Il faudrait alors s'attendre à trouver de préférence les épithéliomas hétérotopiques là où la métaplasie elle-même est fréquente.

En réalité il n'en est pas toujours ainsi.

Les épithéliomas malpighiens des *bronches* ne sont pas rares mais ils sont peut-être moins nombreux que la fréquence de la métaplasie ne le fait supposer. Si l'on considère, d'un côté, le nombre considérable des malades atteints de pneumopathies chroniques avec métaplasie malpighienne des bronches et qui restent indemnes de cancer, de l'autre côté, le nombre surprenant de malades atteints de cancer bronchique et qui n'ont jamais manifesté une atteinte inflammatoire antérieure broncho-pulmonaire, la métaplasie pavimenteuse des bronches cesse de figurer parmi les lésions précancéreuses (R. Huguenin).

Pour le *corps thyroïde*, les faits sont encore plus nets; alors que la métaplasie malpighienne y est relativement fréquente, les cancers malpighiens sont d'une grande rareté. Nous en avons trouvé une quinzaine de cas seulement dans la littérature (Kocher, Ribbert, Demme, Schmidtman, Eppinger, Lucke, Herrenschildt, Masson, Reinstaller). Encore n'est-il nullement prouvé que tous ces cas relèvent réellement d'un processus métaplasique car le corps thyroïde est indiscutablement un siège d'inclusions malpighiennes congénitales (kystes dermoïdes dérivés du canal thyroïdologique des fentes bronchiales, etc. . . .) qui peuvent tout aussi bien être le point de départ d'épithéliomas hétérotopiques.

La vésicule biliaire est sans conteste un des sièges de prédilection des épithéliomas malpighiens hétérotopiques (environ cinquante cas ont été publiés, dont deux personnels). Or, précisément dans la vésicule biliaire les processus métaplasiques sont d'une extrême rareté. Malgré des recherches nombreuses la métaplasie malpighienne n'y a été observée qu'une seule fois, par Lubarsch. Dans le *pancréas*, par contre, où les processus métaplasiques sont fréquents, les épithéliomas malpighiens sont beaucoup plus rares, sept cas seulement se trouvent signalés dans la littérature (Israël, Levisohn, Kawamura, Papadopoulos, Herxheimer, Oberling, Plenge); d'autre part, on a

observé dans le tube digestif des épithéliomas malpighiens dans des régions où l'on n'a jamais constaté de métaplasie, par exemple dans *l'estomac* (Eppinger, Rolleston, Rörig, Calderara, Lubarsch, Pollack, Herxheimer, Borst, Borrmann, Oberling et Wolf, de Martel, Oberling et Pernet) et dans le colon (Schmidtman, Herxheimer, Probst, Plenge).

Dans *l'épididyme*, où les processus métaplasiques sont très fréquents, les cancers sont très rares en général et les épithéliomas malpighiens sont exceptionnels; nous n'avons eu connaissance que d'un seul cas publié par Rowland Nicholson.

*L'utérus* par contre, très rarement atteint de métaplasie est fréquemment le siège d'épithéliomas malpighiens. Cette simple énumération montre qu'il

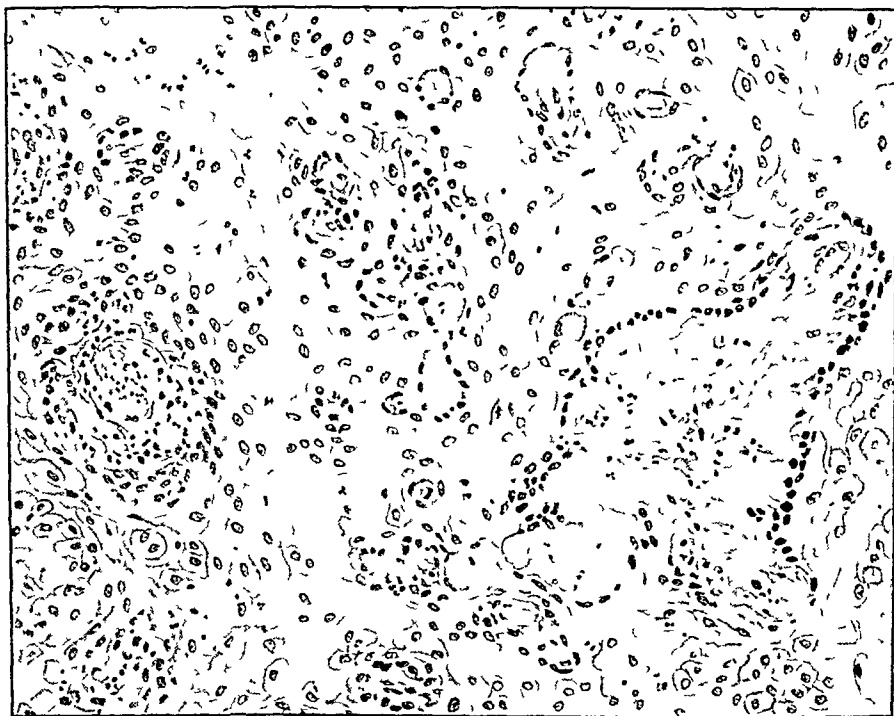


FIG 3 —Épithélioma pavimenteux des plexus choroides. Papilles tapissées par des cellules polygonales de type malpighien

n'y a aucune coincidence entre la fréquence de la métaplasie malpighienne et la fréquence des tumeurs malpighiennes hétérotopiques.

Cette constatation qui paraît surprenante au premier coup d'œil s'explique lorsque l'on étudie de plus près la structure des tumeurs hétérotopiques.

Beaucoup d'entre elles en effet, montrent une structure mixte, à la fois malpighienne et cylindrique. Ce sont ces épithéliomas que les auteurs allemands désignent sous tel nom "d'adénocancroïdes."

Nous avons eu l'occasion d'observer récemment trois de ces tumeurs situées dans le corps utérin et qui peuvent servir d'exemple pour l'étude histologique de ces néoplasmes.

Dans le premier cas, il s'agissait d'une tumeur assez volumineuse, à surface bourgeonnante, occupant la partie supérieure du canal cervical, remplissant la cavité utérine.

## MÉTAPLASIE ÉPITHÉLIALE

A l'examen histologique, on est frappé de voir dans cette tumeur deux structures absolument différentes. Dans sa partie inférieure le néoplasme offre l'aspect d'un épithélioma baso-cellulaire du col utérin, dans sa partie supérieure, celui d'un épithélioma cylindrique. Aux deux extrémités, ces deux structures sont absolument pures; ce n'est que dans la partie centrale du néoplasme où l'on assiste à une intrication des parties pavimenteuses et cylindriques.

Les deux autres cas sont des tumeurs qui, du point de vue macroscopique, réalisent l'aspect habituel du cancer du corps utérin: L'aspect histologique, identique dans les deux cas est très particulier. C'est l'image d'un épithélioma cylindrique parsemé d'innombrables îlots malpighiens; ces îlots sont absolument indépendants les uns des autres, ils se forment aux dépens de l'épithélium cylindrique qui change de forme, donne naissance à un amas de cellules qui fait saillie à l'intérieur du tube. Certaines de ces masses sont formées par des cellules polygonales qui ne présentent aucun attribut spécifique des cellules malpighiennes; dans d'autres, par contre, on voit apparaître des filaments d'union et des gouttelettes de kératohyaline. On voit même des cellules qui s'imbriquent, se disposent en couches concentriques autour d'une gouttelette de kératohyaline et esquissent ainsi la formation d'un globe corné.

Cette répartition différente des zones pavimenteuses et cylindriques que nous avons trouvé dans ces épithéliomas du corps utérin se rencontre également dans les épithéliomas de la vésicule biliaire, de l'estomac, du colon, bref, partout où des tumeurs hétérotopiques ont été signalées.

Ainsi ces épithéliomas à structure mixte peuvent réaliser deux aspects différents: tantôt les parties cylindriques et pavimenteuses sont nettement distinctes, tantôt la structure pavimenteuse apparaît un peu partout dans le domaine d'une tumeur dont la structure fondamentale est cylindrique glandulaire.

L'interprétation sera différente dans les deux cas. Dans la première éventualité, certains auteurs admettent l'existence de deux tumeurs différentes avec intrication secondaire. Le fait serait alors à rapprocher des cas où il y a manifestement association, en une même région, de deux tumeurs différentes comme par exemple d'un épithélioma et d'un sarcome; soit qu'il s'agisse de l'effet du hasard, soit que l'une de ces tumeurs ait déclenché la formation de l'autre. En ce qui concerne notre observation, on peut également penser que la cancérisation a intéressé la muqueuse préalablement métaplasiée et la muqueuse cylindrique située au voisinage.

Dans le deuxième cas il paraît évident que *la métaplasie s'est établie dans la tumeur en évolution*. Cette constatation est très importante car, étant donné le fait que les épithéliomas hétérotopiques se développent fréquemment dans des régions où la métaplasie est rare ou inconnue, il est permis de penser que, dans bien des cas, *la métaplasie ne précède pas le cancer mais qu'elle en est une conséquence*.

Ainsi, l'étude minutieuse des épithéliomas hétérotopiques n'est guère favorable à la thèse suivant laquelle la métaplasie doit être considérée comme une lésion précancéreuse.

Un autre fait vient encore restreindre l'influence de la métaplasie : dans la genèse de certains épithéliomas hétérotopiques : c'est le rôle des malformations embryonnaires.

Certaines hétérotopies congénitales peuvent occasionnellement devenir le point de départ de tumeurs malignes.

Nous figurons ici, à titre d'exemple, un épithélioma qui s'est développé dans le tiers supérieur de l'œsophage chez un homme adulte. Cette tumeur reproduit la structure caractéristique d'un épithélioma gastrique du type de la limite plastique. On voit dans un stroma très développé des cellules isolées ; assez volumineuses, arrondies ou ovoïdes, remplies de gouttelettes de mucus. Dans le domaine de cette tumeur, la muqueuse œsophagienne se trouve interrompue par un îlot gastrique, reproduction fidèle de la muqueuse pylorique.

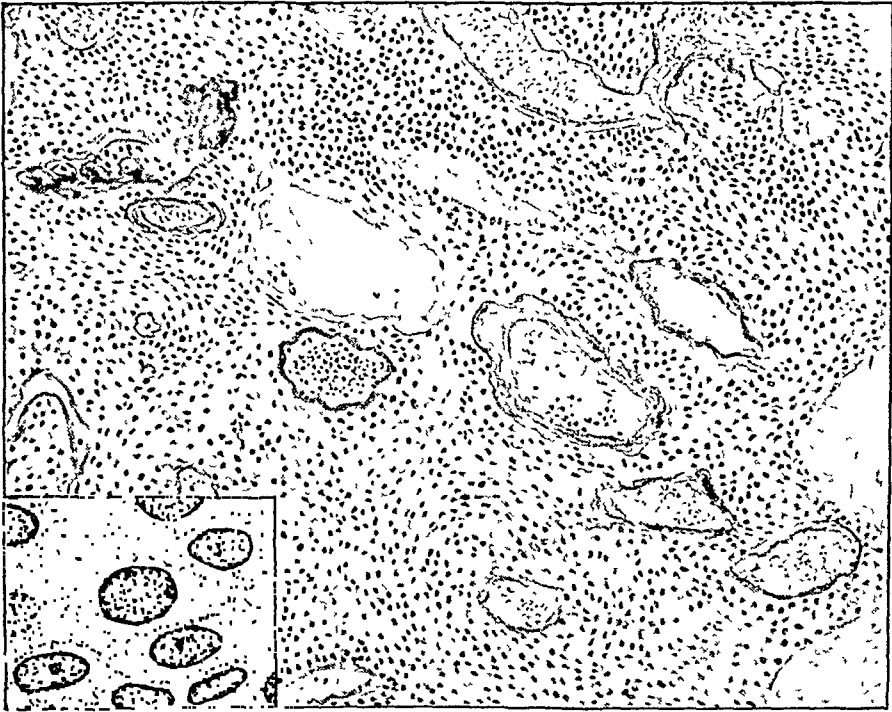


FIG. 4.—La même tumeur, région compacte.

Il paraît donc infiniment probable que cette tumeur a pris naissance aux dépens d'un îlot gastrique semblable, et personne ne songerait ici à soulever l'hypothèse d'une métaplasie.

Or, cette même interprétation s'impose lorsqu'une tumeur malpighienne se développe dans une région où la métaplasie est inconnue, et où l'existence de malformations embryonnaires est démontrée.

Tel est le cas des épithéliomas pavimenteux des plexus choroïdes.

C'est dans le travail de Boudet et Clunet que, pour la première fois, l'attention a été attirée sur ces tumeurs. Ces auteurs décrivent une tumeur papillaire, développée à la base du crâne, et adhérente au cerveau au niveau de la fente de Bichat. L'examen histologique montre de nombreux axes conjonctivo-vasculaires tapissés par un épithélium malpighien à évolution cornée incomplète qui présente des altérations secondaires multiples et variées.

Boudet et Clunet donnent un aperçu bibliographique très complet d'où il ressort que des tumeurs malpighiennes ont été observées à différentes reprises dans le domaine de l'encéphale—notamment à la base du crâne, dans le troisième et dans le quatrième ventricule.

Un autre cas d'épithélioma malpighien du troisième ventricule a été décrit par I. Bertrand en 1924, et nous avons l'occasion d'y ajouter une nouvelle observation concernant un homme de vingt-six ans.

Au microscope, la tumeur montre une structure papillaire; on voit des axes conjonctivo-vasculaires tantôt grêles et délicats, tantôt épais et scléreux, tapissés par un revêtement malpighien caractéristique. Celui-ci présente des aspects un peu différents suivant les points. Dans certaines régions les cellules ont tendance à s'écarter, seules les cellules de la couche basale, qui se trouvent au contact du tissu conjonctivo-vasculaire, restent serrées les unes contre les autres; elles se distinguent des autres par leur taille réduite—ce sont des éléments cylindro-cubiques—et par la basophilie de leur cytoplasme.

Dans d'autres régions, le tissu néoplasique est plus dense, les cellules se tassent les unes contre les autres, forment des plages plus ou moins étendues, interrompues seulement par des axes conjonctivo-vasculaires. Les cellules, à ce niveau, montrent l'aspect caractéristique des cellules malpighiennes: elles sont réunies entre elles par des filaments d'union et, ça et là, on remarque des boules de kératohyaline.

A l'autopsie, la base du cerveau paraît nettement bombée dans la région de l'infundibulum. En pratiquant des coupes frontales, on se rend compte que le troisième ventricule est rempli d'une masse tumorale anfractueuse de la grosseur d'une noix. La tumeur a fortement distendu les parois ventriculaires, les couches optiques sont écartées mais le tissu cérébral environnant n'est nullement infiltré. Les deux ventricules latéraux sont considérablement distendus mais indemnes de néoplasme.

Peut-on incriminer dans la genèse de ces néoplasmes un processus métaplasique? Nous ne le croyons pas, et pour les raisons suivantes:

(1) La métaplasie, dans le domaine de l'encéphale (plexus choroïdes, épendyme), n'a jamais été observée.

(2) Ces tumeurs se développent sans exception, au voisinage de la base du crâne, (troisième ventricule de préférence), dans une région où l'existence d'hétérotopies malpighiennes a été démontrée à de multiples reprises.

(3) Ces tumeurs s'observent souvent chez des sujets jeunes (Cas Mott et Barrat, trente-quatre et vingt-huit ans, cas Saxer quarante-six ans, cas Bergmann et Steinhaus sept ans, cas Mackay et Bruce seize ans, cas Boudet et Clunet huit mois, cas Bertrand cinquante ans, cas personnel vingt-six ans).

Il semble donc logique d'admettre que ces tumeurs ont eu pour origine une hétérotopie congénitale, mais ce fait n'implique à notre avis aucune interprétation pathogénique. La malformation embryonnaire n'explique pas la *genèse*, mais uniquement la *structure hétérotopique* de la tumeur—elle n'est pas une lésion précancéreuse, pas plus que la métaplasie. La preuve réside précisément dans ce fait que certaines malformations telles que les

îlots gastriques de l'œsophage sont extrêmement fréquentes alors que leur transformation cancéreuse est très rare. Cela prouve que dans l'interprétation histogénétique des tumeurs hétérotopiques un certain éclectisme est nécessaire.

# CONCLUSIONS

Certaines muqueuses cylindriques sont fréquemment le siège d'une métaplasie malpighienne, mais dans aucune de ces régions le pourcentage des tumeurs malpighiennes ne devient prédominant; dans plusieurs de ces régions même, les épithéliomas malpighiens sont remarquablement rares. On ne peut donc pas considérer la métaplasie comme une lésion précancéreuse.

Bien souvent par contre, la métaplasie ne s'extériorise que dans une tumeur en évolution; elle est alors consécutive à la cancérisation. Ce fait s'observe notamment dans certains organes tels que la vésicule biliaire et l'utérus où la métaplasie malpighienne, en dehors des tumeurs, est extrêmement rare.

Il en résulte que, du point de vue pratique, l'interprétation de la métaplasie épithéliale doit varier suivant les organes. Dans les bronches, dans le pancréas, dans l'épididyme, la métaplasie n'est nullement l'indice d'une cancérisation imminente, tandis que dans l'utérus, la présence d'îlots malpighiens est souvent le signe d'une cancérisation déjà établie.

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# TREATMENT OF MALIGNANCY

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NO ONE can write adequately of any phase of the problems presented by malignant disease without acknowledging his debt to James Ewing. While the surgeon is primarily concerned with the possibilities of the removal of an invaded tissue, in the matter of the extent of operation in each case he must be guided by his decision as to whether the growth is truly benign, premalignant or frankly malignant. Doctor Ewing's purpose, as expressed in his preface, is to contribute something toward the reduction of mortality from cancer. Since it is only by increasing knowledge of the nature of cancer that mortality from this disease can be reduced, he has certainly made a great contribution toward the attainment of this purpose. Ever since the appearance of the first edition of "Neoplastic Diseases" in 1919, my associates and I have constantly made use of the wealth of information contained in that and in the succeeding editions.

While neither the cause of malignant disease nor its cure has yet been found, despite world-wide researches and vastly extending clinical experience, nevertheless great progress toward the conquering of this scourge of the human race has been made by the disproof of many false theories, by the discrediting of many so-called "cures," the studies of the incidence of malignancy in relation to age, race, climate, and the different bodily tissues, by investigations of its method of growth, and by the observation of the effects upon it of various physical and chemical agents. From all of these studies the practical results have been meager. We have learned, however, that cancer, whether of the external and visible parts or of the internal, invisible organs, obeys one general law of growth, and the old dictum based entirely upon clinical experience is established more uniformly than ever—namely, that the one and only cure for cancer is its early and complete removal. It is probable that with extending knowledge of the operation of physical laws in biological processes, new light may be thrown upon the causation of malignant growths, and that from this knowledge new methods of cure may be evolved. Already, investigations have shown that the electric capacity and conductivity of cancer of any part far exceeds the capacity and conductivity of the normal tissue, while the potential in cancer is opposite to that in normal tissue. The histologic appearance of a cancer offers a static picture of the cells. The capacity and potential measurements present the dynamic status of the cells, and it is with the dynamic status of the cells that we are primarily concerned in interpreting the status of any malignant or pre-malignant condition.

Whatever these and other researches may disclose to us in the future, at present the one sure method of approach to the cancer problem is that



based upon clinical experience. I propose, therefore, to offer in this paper a review of the methods employed by my associates and myself in dealing with cancer of the various tissues, these methods being based upon our experience in 7,390 cases of malignancy.

It is of interest to note, in regard to cancer of the external parts, that, to my knowledge, no case of cancer has been observed on the normal, uninjured skin. The skin of the face, in particular, offers an opportunity for the study of the natural development of cancer which is of greater value than that of any condition induced in the laboratory. I have never seen a cancer develop upon the healthy skin of the face. It is always preceded by a pre-cancerous stage, a keratosis, a mole or wart, a benign tumor or ulcer. The pre-cancerous history is often a long one—of little scales picked off as frequently as they recurred, of a wart goaded by constant picking. In the case of a cancer on the buccal surfaces also there is usually a history of trauma from a rough tooth, from leucoplakia, or a fissure.

If in the cancer period of life every unhealthy scar were excised and the surface covered by skin grafting, if every chronic irritation were removed, if every ulcer were healed soundly, or excised and the surface covered by skin grafting, if every wart and mole were excised, if the mouth were kept wholesome, the teeth smooth and even, it would be found that the problem presented by cancer of the outer surfaces of the body would be well-nigh solved.

Since cancers obey one general law of growth, we may be sure that cancers of the inner, hidden parts follow the same course as do cancers of the skin. We must conclude, therefore, that internal cancers have their pre-cancer stages—chronic irritation, ulcerative benign growths, etc. Thus in the larynx the pre-cancerous state may be a syphilitic ulcer or a papilloma; in the stomach it may be a chronic ulcer; in the gall-bladder, irritating gall-stones and chronic inflammation; in the large intestine and rectum, ulcers and irritation from various sources; in the breast, chronic inflammation, benign tumors of certain types and senile changes; in the uterus, the irritations of pregnancy and senile changes, and benign growths; in the kidney and bladder, stones and benign growths.

Unfortunately, not all pre-cancerous conditions of the internal organs are amenable to treatment, but to the extent that these pre-cancerous states may be corrected, to that extent will the problem presented by cancer of these parts be solved.

Once the pre-cancer stage has passed, then complete removal of the growth—whether by excision, or by the X-ray or radium—becomes the only safe procedure. It is interesting and encouraging to note that increasing numbers of patients consult the surgeon as soon as any symptoms are presented which indicate an abnormal condition of any organ or tissue; in consequence, the percentage of cases of cancer which are caught in their early stages is increasing. Unfortunately, however, some of these internal cancers are symptomless in their earliest stages, so that when they come to operation

they are so far advanced that even if removal of the local growth is still possible, there is danger that distant metastases are present.

It remains to discuss the treatment most preferred by my associates and myself for cancer of the various organs and tissues.

*The Skin.*—In our experience in the treatment of 629 cases of carcinoma of the skin and subcutaneous tissues, we have found that radium is the most efficient treatment, except in the case of a pigmented mole, which should always be excised.

*The Jaws and Buccal Surfaces.*—Our records include 549 cases of carcinoma of the buccal surfaces and jaw. Among these, 21.3 per cent. were cases of carcinoma of the tongue, 43.3 per cent. were carcinomata of the lip, and 13.3 per cent. were carcinoma of the jaw. Among the cases on which we have follow-up data, 25.37 per cent. have lived for five years or more.

Some years ago a study of 4,500 reported cases of cancer of the head and neck was made for me by Dr. F. W. Hitchings, who found that in less than 1 per cent. of these cases secondary cancer foci were found in distant organs and tissues. In cases of cancer of the head and neck, therefore, death, when it occurs, is almost invariably the result of the local development of the disease, the reason for this localization being the extraordinary barrier formed by the collar of lymphatics in the neck, every portion of which is readily accessible to the surgeon. Above this lymphatic collar, however, metastases are rapidly disseminated. In contradistinction to cancer of the skin and superficial parts which metastasize late, and are effectively treated by the local application of radium and the X-ray, cancer of the buccal surfaces demands the complete removal of the glands of the neck on both sides. In early cases of cancer of the jaws, on the other hand, since this condition metastasizes slowly, and usually only on the side of the lesion, a less radical operation is indicated, but in the advanced cases of cancer of the jaws, a wide regional block dissection is indicated.

As for the removal of the primary focus, an early cancer of the lip is usually successfully treated by radium; early cancer of the tongue or of the buccal cavity may be treated by radiation, or perhaps better by electrocoagulation. Every case of advanced cancer of the lip or tongue should be excised, and as stated above, the lymphatic glands of the neck should also be removed by wide block dissection. In cases of carcinoma of the jaws a "platter" of underlying bone should be removed together with the intact growth.

It should be emphasized that while radiation of the local lesion may be indicated, radiation of the involved lymphatic glands of the neck should never be done, as this treatment cannot be depended upon. If the glands of the neck have been irradiated and the patient has recovered, we must conclude that the glands of the neck probably were not involved. After operation on any part of this field, post-operative treatment with deep, accurately measured X-ray or radium radiation is of advantage. Always in these cases

should be borne in mind the prime importance of the minimum handling of the carcinomatous tissue and the avoidance of the implantation of cancer cells in the operative field.

*The Larynx.*—Our series includes 134 cases of carcinoma of the larynx, in fifty-seven of which operation was performed. Among those patients on whom we have follow-up data, 63.2 per cent. have survived for more than five years.

Cancer of the larynx calls for laryngectomy, which is one of the most successful operations for the permanent cure of cancer. Here, as nowhere else in the body, except in visible parts, the presence of cancer is evident in its earliest stages, for it is announced by every spoken word of the patient. Moreover, in cases of intrinsic cancer of the larynx there is practically no lymphatic involvement, for the reason that intrinsic cancer of the larynx is, as it were, confined in a box through whose walls the cancer cannot penetrate, for cancer cannot penetrate through hyaline cartilage. There is no other situation in the body in which cancer declares itself immediately and from which it cannot be disseminated into the lymphatic glands. If a cancer of the larynx is extrinsic, then because of the abundance of lymphatic connections, it will extend rapidly, and generally operation is, at best, only a palliative remedy. In such cases the only hope lies in the local removal of the growth and block dissection of the gland-bearing area. In operable cases in which only tracheotomy can be attempted, radium is of value as a palliative measure.

For intrinsic cancer of the larynx, as stated above, laryngectomy is indicated, the general trend of opinion being against the use of radium, for laryngectomy offers a practical certainty of cure, provided the cancer is entirely intrinsic. The post-operative application of the X-ray, however, may be of value, as it may check any extension of the growth provided some undiscovered extrinsic focus exists, or provided some cancer cells have become implanted.

*The Thyroid Gland.*—In our total series of thyroidectomies, there has been a carcinoma of the thyroid gland in 268 cases. In about 90 per cent. of these cases the carcinoma was due to the degeneration of an adenoma. For this reason I believe that all adenomata should be removed. Thus the treatment of carcinoma of the thyroid gland, like the treatment of goitre, is mainly a problem of prevention. If the case is operable, there is no question as to the treatment; the only difficulties are presented by the inoperable cases in which the patient is suffering from obstruction and partial asphyxiation. In such a case the implantation of radium is indicated, together with a decompression operation if the distress of the patient demands immediate relief. In this operation the preglandular muscles are divided, thus relieving the back pressure of the gland upon the trachea.

Sometimes as the result of radiation the carcinoma will disappear; in other cases radiation seems to be of no avail. Radiation may produce myxoedema, but this is readily overcome by the administration of thyroid

extract. What the end-result of decompression and radiation may be in any given case cannot be foretold, but the patient is certain to have a period of relief. It must be borne in mind that involvement of the neighboring tissues is almost sure to be present, and that if the cancer involves the trachea there is practically no hope of cure.

*The Œsophagus.*—Our total series includes 111 cases of cancer of the œsophagus, in the majority of which the symptoms had been present for less than six months. This is one of the most hopeless of malignant conditions, for when the patient presents himself it is usually too late for surgical treatment to be of any value. The emaciation and weakness due to the dysphagia, which is the prominent symptom, in itself makes every case a poor surgical risk. In most of our cases dysphagia was already so marked as to have produced extreme emaciation and exhaustion.

None of the cases of cancer of the œsophagus in our series have survived for more than thirty-four months.

*The Breast.*—Our total series includes 1,350 cases of cancer of the breast, fourteen in males. In 789 cases the patients have been treated by surgery alone; in 398 by surgery and radiation. Of the patients regarding whom we have follow-up data, 25.70 per cent. have survived for five years or more.

According to Ewing, the United States Census for 1914 reported 5,423 deaths from cancer of the breast among 52,420 total cancer deaths, an incidence of over 10 per cent.<sup>1</sup> I am inclined to believe that the 1930 census will present a lower incidence, since, as the result of increasing knowledge on the part of the laity of the symptoms of the early stages of cancer, especially of cancer of the breast, the number of patients who present themselves with inoperable cancer of the breast is constantly diminishing. The majority of women are now ready to consult their physician upon the first appearance of any abnormality in the breast.

The problem for the surgeon, therefore, has become one of accurate differentiation between benign and malignant tumors. Frank cancer is easily diagnosed, but the diagnosis of border-line cases is by no means a simple problem. Bloodgood at one time submitted specimens from over sixty border-line cases to a number of pathologists. These pathologists were divided into two groups, one of which favored a diagnosis of cancer, the other believed the growth to be a benign lesion. "In not a single case has there been a uniform agreement as to whether the lesion was benign or malignant."<sup>2</sup>

Ewing states that "the great majority of mammary cancers are rather easily recognizable by inspection and palpation."<sup>3</sup> In cases in which the clinical symptoms and the frozen section cannot give absolute proof of the character of the tumor, the utmost safety of the patient demands the complete excision of the breast and of the regional lymphatics, for unlike cancer of the head and neck or the imprisoned, intrinsic cancer of the larynx, the abundant, lymphatic channels from the breast may readily and easily produce thoracic and abdominal metastases.

Among the so-called benign breast lesions which are possibly pre-cancerous are diffuse hypertrophy, traumata, chronic mastitis, and cysts, as well as the so-called benign tumors.

In regard to the so-called benign tumors, Deaver has stated, "Tumors of certain types having certain structure are constantly harmless; those of other types, having another structure, are persistently invasive, destructive and constantly fatal. Unfortunately these are the extremes of a series between which lie many tumors that may or may not be harmful, or whose structures may fail to give a clue to their true disposition."<sup>4</sup> I am far from recommending the radical operation in every case of tumor of the breast, but I do wish to emphasize the importance of frequent examination of the breast after the local excision of what appears to be a benign tumor, so that the radical operation may be performed immediately if the lesion shows any suspicion of malignancy. A biopsy should never be performed, for if the growth should prove to be malignant there is danger of its dissemination, and whatever its character, in any case it should be removed entirely and then sectioned.

As for the rôle of radiation—from a study of the end-results in our series, Portmann draws the following conclusions:<sup>5</sup>

"1. Intensive X-ray therapy, especially by the cross-fire method, is not the preferred procedure or the post-operative treatment of carcinoma of the breast.

"2. Post-operative X-ray therapy by moderate repeated dosage decreases the number of recurrences and metastases, and prolongs the life of many patients suffering from carcinoma of the breast."

We, therefore, give radiation therapy as soon as possible after operation, not waiting until the wound is healed. Only if a case is entirely inoperable is radiation employed as a palliative measure instead of surgery.

*The Stomach.*—A study of the records of our 648 cases of cancer of the stomach shows that the history is commonly a history of indigestion or of ulcer; that ulcer of the stomach has a distinct potentiality as a pre-cancerous condition; that the history and the X-ray findings are the most valuable means of diagnosis; that a differential diagnosis between an old ulcer and early cancer cannot be made with certainty; that when the probability of cancer is suspected an exploration should be made at once. In late cases, as in late cases of cancer elsewhere, even though the operation is survived and the local lesion removed, there is great danger of metastases, especially in the liver or retroperitoneal glands.

A cancer of the stomach is characterized by such a rapidity of growth and such an extent of lymphatic involvement that an inoperable stage is reached very early in its progress. Since the earliest stages are practically symptomless, and the earliest symptoms are those of more or less mild indigestion, in the majority of cases the patients come too late for possible cure.

The operation indicated is the widest possible excision of the growth,

and the patient should be offered every safeguard and aid that surgery has to offer. By the use of blood transfusion, saline injections, diathermy during and after the operation, the application of hot packs, and a divided operation in many cases in which the prognosis appears to be hopeless, the patient may be carried through to cure or to a comparatively comfortable prolongation of life. In regard to the divided operation, it may be added that in certain cases in which the diagnosis of cancer has been made, the supposedly cancerous mass has disappeared in the interval between the two stages so that the second stage has not been required.

Among our cases of cancer of the stomach, of those patients on whom follow-up data are available, 4.44 per cent. have passed the five-year period. Resections have been made in ninety-five cases with five-year survivals in 6.94 per cent.; gastroenterostomy in 168, with five-year survivals in 5.21 per cent.; and radiation therapy alone in twenty with no five-year survivals. In the last two instances, perhaps our diagnosis may be questioned, but in each of these cases the clinical signs, the X-ray picture and the exploratory operation gave every evidence of an inoperable carcinoma.

*Gall-bladder.*—Our records include sixty-four cases of carcinoma of the gall-bladder and bile-ducts among which operations were performed in twelve cases. We have a record of two five-year survivals.

If a patient presents symptoms referable to the gall-bladder of more than one year's duration, the possibility of malignancy of the gall-bladder should be considered. Cancer of the gall-bladder is usually associated with cholecystitis, and consequently in many cases the patient is treated for the latter condition until the disease has extended into the liver and deep structures. Then when its malignant character is recognized, it is too late for operation to be of any avail. If the presence of the malignant condition is recognized before extension to the liver has occurred, then an immediate cholecystectomy is indicated.

*The Liver.*—Of cancer of the liver it is necessary to state only that it is rarely primary and is always incurable. Only palliative efforts can be made and their effect at best is but temporary. Our records include 103 cases of cancer of the liver, among which three were shown at autopsy to be primary.

*The Intestines and Rectum.*—Our total series of cases of carcinoma of the large intestine and rectum includes 685 cases. Of the cases in regard to which we have follow-up data, 8.45 per cent. have survived for five years or more.

The diagnosis of carcinoma of the small intestine is made from the history and clinical signs and the X-ray picture. If the presence of a cancer is indicated then an exploratory operation should be performed to determine operability, with immediate removal of the growth if possible. As in the case of carcinoma of the stomach, every available method for the conservation and restoration of the patient should be employed. Our records include twenty-one cases of carcinoma of the small intestine.

In cases of carcinoma of the large intestine and rectum, a colostomy should be performed, followed by radical operation, X-ray radiation being

employed after the operation. In cases in which the growth is so low in the rectum as to be readily accessible, the implantation of radium needles and the application of radium packs may be sufficient. In inoperable cases a colostomy should be done, followed by radiation. There should be a period of about ten days between the colostomy and the final operation, or rather, between the colostomy and the decision as to the method of treatment, as a period of that length is necessary to allow the inflammatory reactions of the disease to subside sufficiently to make it possible to determine what operation shall be performed. This decision depends, of course, upon the findings of an exploratory operation. The entire picture may change during this period.

While the application of deep X-ray radiation is beneficial after operation or after radium treatment, it is of little, if any, value in the treatment of recurrences.

A statistical study of cases treated at the Cleveland Clinic since 1921 shows the following survival percentages:

CANCER OF THE RECTUM AND SIGMOID

| Treatment                         | Total cases | Traced cases | Survival more than five years |
|-----------------------------------|-------------|--------------|-------------------------------|
| Resection . . . . .               | 145         | 125          | 7.2 per cent.                 |
| Resection and radiation . . . . . | 39          | 34           | 20.6 per cent.                |
| Colostomy only . . . . .          | 108         | 63           | 0 per cent.                   |
| Colostomy and radiation . . . . . | 76          | 70           | 10 per cent.                  |
| Radiation only . . . . .          | 36          | 27           | 7.4 per cent.                 |

These figures show, as Jones<sup>6</sup> has reported, that although operation by the abdomino-perineal route, combined with radiation, is the treatment of choice, if operation is refused or if the condition is inoperable, there is sufficient evidence that a cure can be obtained in certain cases and marked palliation in others by the use of radium and Röntgen-ray.

*The Genito-urinary Organs.*—The records of Doctor Lower and his associates at the Cleveland Clinic include 805 cases of malignant disease of the genito-urinary organs—335 of the bladder, 124 of the kidney, 16 of the urethra, two of the ureter, 268 of the prostate, and 60 of the testicle.

Among these cases in which the results are known, there have survived for five years or more 9.84 per cent. of the cases of malignant disease of the bladder, 8.74 per cent. of the cases of malignant disease of the kidneys, 3.75 per cent. of the cases of carcinoma of the prostate.

In general, malignant tumors of the genito-urinary organs are best treated by surgery with the addition of radiation in certain cases. In inoperable cases, radiation may be the only available method of treatment.

In some cases, tumors of the kidney in children may be reduced by deep X-ray therapy, but the radiation must be followed later by surgery.

For malignant tumors of the kidney in adults, the indicated treatment is surgery with radiation both before and after operation. In many cases radiation will so reduce the size of the tumor that cases which have seemed to be inoperable become operable. Tumors of the kidney should be irradiated

no matter how hopeless the outlook. In the case of deep-seated bladder tumors, radium has seemed to prevail in certain cases, but the results are too uncertain for radiation to be used routinely. Post-operative radiation is employed in many cases, but principally because of the hope that it may be of avail rather than because of any definite results that have been secured up to the present time.

Malignant tumors of the testes are treated by surgery with radiation both before and after operation.

Whether or not prostatectomy or radiation is the preferred treatment for carcinoma of the prostate remains to be decided. We believe that prostatectomy is to be preferred in uncomplicated cases, but we know that in cases in which a high blood urea cannot be reduced, radiation may provide the only possible method of treatment, or it may tide the patient over until prostatectomy can be performed.

*The Uterus.*—Our records include 783 cases of carcinoma of the uterus. Of the 211 cases of carcinoma of the fundus, 14.84 per cent. of those patients on whose cases we have follow-up data have survived for five years or more.

Of the 572 cases of carcinoma of the cervix we have follow-up data in 208 cases treated by radiation, and in 129 cases treated by surgery, before we adopted our present policy—9.13 per cent. of the former and 17.05 per cent. of the latter have survived for five years or more.

The preferred treatment of carcinoma of the fundus still seems to be *sub judice*—both as to whether surgery or radiation is the treatment of choice, and as to the type of operation to be performed.

As to carcinoma of the cervix, on the other hand, the preëminent value of radiation appears to be established. At the Cleveland Clinic we now use radiation rather than surgery in the treatment of carcinoma of the cervix, reserving our final judgment until sufficient time has elapsed for a definite comparative study of the end-results.

As the presence of any but a frankly benign tumor of the breast demands the removal of that organ, especially in a patient past middle age, so when an intermittent or continuous uterine discharge occurs in a patient who has passed the menopause, we believe that a complete hysterectomy should be performed at once. Even if the character of the discharge does not appear to indicate the presence of a malignant condition, this operation should be performed without delay. In such cases curettage is contra-indicated, as, if cancer is present, the cancer cells will be disseminated.

In inoperable cases of carcinoma of the fundus, deep X-ray therapy is of value as a palliative agent and for the prolongation of life.

In the treatment of carcinoma of the cervix, both radium and deep X-ray therapy are used, the former being applied in needles and by radium packs.

*Ovary.*—We have seen 128 cases of carcinoma of the ovary. This growth is rarely primary, and in cases in which it is primary the removal



of both ovaries is indicated. If the peritoneum is extensively involved, deep X-ray therapy may retard the progress of the disease.

There have survived, for five years or more, 7.57 per cent. of our cases.

*Bone.*—Exclusive of carcinoma of the jaw, we have seen 161 cases of malignant disease of bone. It is still uncertain whether a primary malignancy of bone should be treated by X-ray or by surgery, but two things are certain: first, if an operation is performed, it should be preceded and followed by X-ray radiation, and second, if the condition is in a limb, amputation should immediately follow radiation, provided the condition is not inoperable. As for metastatic tumors, palliative treatment by the X-ray is the only therapeutic measure. Radium is contra-indicated as it would destroy the periosteum, and necrosis would follow.

The data which are being accumulated by the Registry of Bone Sarcoma of the American College of Surgeons may finally lead to a decision as to the relative merits of surgery and of radiation in the treatment of malignant diseases of bone.

Malignant tumors of other tissues might be included in this discussion, but in some instances they are exceedingly rare; in others they are practically never primary; in some they belong in the domain of the specialist. We shall only add here that in these cases the same rule applies as in those we have discussed above, that is, removal of the tumor by the most effective method if the site and extension of the tumor and the condition of the patient permit.

Finally, it may be emphasized that, whatever his present point of view regarding the method of choice in the treatment of a malignant tumor of any organ or tissue, the surgeon must hold himself in readiness to alter that view if accumulating experience indicates that other methods are to be preferred or are at least worthy of trial. It may be that as the result of the researches—clinical and experimental—which are in progress in many clinics and laboratories, some new and effective measure may be developed of which we should be ready to avail ourselves.

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# EPIDERMOID CARCINOMA IN SEBACEOUS CYSTS

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OF ATLANTA, GA.

FROM THE DEPARTMENT OF PATHOLOGY OF THE STEINER CANCER CLINIC

THE very common sebaceous cyst or "wen" is usually considered a very harmless lesion. However, it is certain that a number of these cysts eventually develop into malignant tumors. Statistics are of comparatively little value, for the vast majority of such cysts are not subjected to microscopical examination following their removal, and in a goodly number of cases, it is the development of a malignant tumor which calls attention to a lesion which may not have been previously observed, or in which little or no evidence of its development on or in a benign cyst can be detected.

Again, cysts may have been removed and there follows after a variable period of time, a recurrence in or near the scar, which recurrent tumor the surgeon is more apt to have examined than the primary cystic mass. That carcinoma does develop in a number of these cysts is well recognized by some writers, for one is able to find a number of references in the literature.

It seems reasonable to assume that a sebaceous cyst would be a fertile field for the development of malignancy when we consider certain factors which are present, and which are recognized as having considerable bearing on the development of carcinoma elsewhere. The formation of the cyst is due to mechanical blocking of the duct followed by retention of secretion. This is accompanied by a continued and increased activity of the cells within the cyst, for it may be that the cells become overactive as a result of the chronic irritation of retained secretion. To this add infection, either acute, chronic, or both, and we have a possible stimulus for the development of a malignant tumor.

Most of the patients with a sebaceous cyst usually give a history of its having been present for a considerable period of time before they seek its removal. Multiple cysts are quite common, and while a number of cases of carcinoma have occurred in patients with multiple cysts, yet multiple carcinomas in such cysts are unusual.

Broders and Wilson<sup>1</sup> reserve the name "sebaceous cyst" for those in which is found sebaceous material, white and granular with an offensive odor, while they designate the firm, solid tumors with lamellated structure as "keratoma." They believe that the latter arise from the lining cells of the duct and not from the gland proper. This would seemingly favor the development of squamous carcinoma, and yet we have been unable to find carcinoma in any "keratoma," all of our cases apparently arising in true sebaceous cysts, with perhaps one exception, one patient applying for treatment with a large recurrent tumor, and the history that "a sebaceous cyst had been removed some-time before."

Ewing<sup>2</sup> mentions the development of carcinoma in sebaceous cysts, with a "structure recalling the cells of the ducts." Caylor<sup>3</sup> reviewed the subject in 1925 and reported twelve cases from The Mayo Clinic. He also called attention to the fact that the actual percentage of malignant tumors is probably higher than it should be because many simple cysts were not sent to the laboratory. He found twelve malignant tumors in a series of 236 cysts, a percentage of 3.44.

In this laboratory 119 cysts and keratomas have been examined. Of this number, eleven showed definite carcinoma, and two others such marked epithelial activity as to be classed as "pre-cancerous." One case was diagnosed clinically as malignant at the time of admission.

FIG. 1.—Epidermoid carcinoma in sebaceous cyst of scalp. Grade I, Case XI.

Apparently the tendency toward malignancy, as in other forms, increases as the patient grows older, although a few cases have occurred in comparatively young individuals. In our series, the average age for all benign cysts was 38.3 years, the youngest patient six and the eldest seventy-six. In the

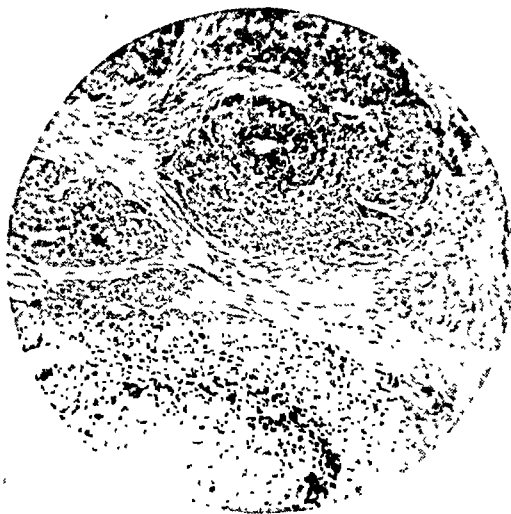


FIG. 2.—Epidermoid carcinoma in sebaceous cyst of scalp. Grade III, Case II.

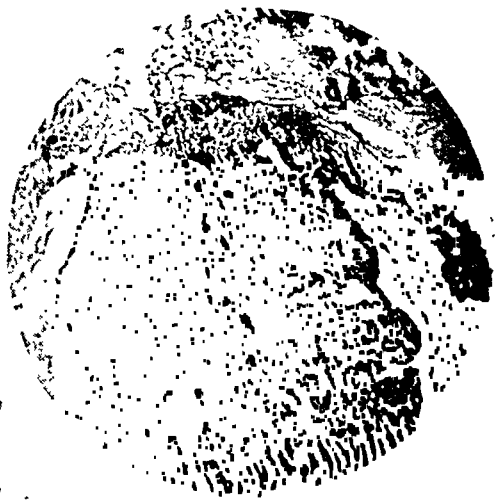


FIG. 3.—Epidermoid carcinoma in sebaceous cyst of arm. Basal cell. Case VIII.

eleven cases of carcinoma, the average age was 64.2 years, the youngest thirty-nine and the eldest eighty-three. All of these patients were over fifty except the one aged thirty-nine. The percentage of carcinoma in the whole series was 9.2. Ricker and Schwalb<sup>4</sup> reported forty-three cases, of which

thirty-nine were over forty years of age. In other reports there are recorded cases of malignancy in sebaceous cysts in patients, thirty-eight, twenty-seven and twenty years of age.

Patients with cysts were almost equally divided as to sex in our series, fifty-four female to fifty-two male.\* However, the proportion of carcinoma in cysts in the female was much greater than in the male, a proportion of 8 to 3. It is interesting to note that there was only one case occurring in a negro, and that one a malignant cyst of the scalp.

The influence of direct trauma in the development of carcinoma in cysts of the scalp may be of some importance in a few of the cases. One of our series gave a history of scratching the cyst with a comb, while another stated that the cyst had been bruised against a table top. However, the other cases gave no definite history of any injury.

As to location, the scalp and face seem to be the more common locations for both simple and carcinomatous cysts. In Caylor's series<sup>3</sup> all but two occurred above the shoulders, while Ricker and Schwalb<sup>4</sup> found the face to be the most frequent location.

Most of the tumors reported by various writers have been of squamous type. A few cases of basal-cell carcinoma are reported, but none of these have occurred in the scalp. The case reported by Narat<sup>5</sup> was a rodent ulcer in the skin *over* a cyst of the scalp but not *in* the cyst itself. Seff and Berkowitz<sup>6</sup> reported two squamous-cell tumors of the scalp and temporal region, and a rodent ulcer of the forehead. Busfield's case<sup>7</sup> was a rodent ulcer developing in a cyst of the forehead, which had been present for a number of years in a seventy-year-old patient, the tumor eventually involving the entire side of the face.

The structure of epidermoid carcinoma in sebaceous cysts varies to a moderate degree. For the most part, the cells are fairly well differentiated, with considerable hornification, pearls and spines. It is possible to find less differentiated areas in many of the tumors, but the proportion of adult structure is usually much greater. The grading of these tumors according to Broder's classification<sup>8</sup> is of considerable value, for the more adult the tumor structure, the slower its growth and the less likely is it to metastasize beyond the nearest nodes. The few cases which have developed generalized metastases have been of undifferentiated types, Caylor's case being graded 4, and the fatal case of Seff and Berkowitz, from the pathological description, a grade 3. Gregersen<sup>9</sup> reports a case with metastasis to the brain, grade unknown. The structure of the few basal-cell tumors has been quite characteristic of that group of tumors, and their course in keeping with such structure.

Recurrences following removal of these tumors are fairly common, especially if the skin is resected close to the tumor edge. In fact, the tumor itself

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\* The total number of cysts is greater than the total number of patients, for several patients had multiple cysts.

TABLE I

*Location of all cysts examined*

|               |    |                       |   |
|---------------|----|-----------------------|---|
| Scalp.....    | 42 | Chest wall.....       | 2 |
| Face.....     | 16 | Breast.....           | 2 |
| Back.....     | 9  | Finger.....           | 2 |
| Ear.....      | 8  | Hand.....             | 1 |
| Forehead..... | 8  | Thigh.....            | 1 |
| Cheek.....    | 7  | Scrotum.....          | 2 |
| Neck.....     | 3  | Nose.....             | 2 |
| Chin.....     | 3  | Arm.....              | 1 |
| Gluteal.....  | 3  | Lumbar.....           | 1 |
| Eyelid.....   | 2  | Location unknown..... | 2 |
| Shoulder..... | 2  |                       |   |

TABLE II

*Epidermoid carcinoma in sebaceous cysts*

| No.                  | Sex | Color | Age | Location | Grade |
|----------------------|-----|-------|-----|----------|-------|
| 1.....               | M   | W     | 50  | Nose     | Basal |
| 2.....               | F   | W     | 83  | Scalp    | III   |
| 3.....               | F   | W     | 60  | Scalp    | I     |
| 4.....               | F   | W     | 72  | Neck     | I     |
| 5.....               | F   | W     | 60  | Forehead | II    |
| 6.....               | M   | W     | 75  | Face     | I     |
| 7.....               | F   | W     | 65  | Scalp    | I     |
| 8.....               | F   | W     | 39  | Arm      | Basal |
| 9.....               | F   | W     | 63  | Cheek    | III   |
| 10.....              | M   | W     | 76  | Scalp    | I     |
| 11.....              | F   | C     | 62  | Scalp    | I     |
| <i>Pre-cancerous</i> |     |       |     |          |       |
| 1.....               | F   | W     | 60  | Scalp    |       |
| 2.....               | F   | W     | 52  | Scalp    |       |

may develop in a small fragment of a cyst incompletely removed. Metastases are comparatively infrequent, in spite of the three cases mentioned above. Our series fails to show any case in which metastases developed, although recurrences occurred in two.

Of the cases here reported, "pre-cancerous" case I died, some time after being seen in this clinic, of carcinoma of the breast with liver metastasis, which disease was present at the time of the removal of the cyst. Case II died three years after being seen, cause unknown. Case III died of pellagra about a year later. The remaining patients were without evidence of disease when last seen, although a few of them have been lost track of.

## CANCER SERVICE IN MASSACHUSETTS\*

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To THE physician in general practice the cancer problem presents itself as perhaps the most difficult, the most distressing, and the most hopeless of all of the many baffling problems with which he has to deal in his daily rounds. The treatment and the care of many diseases is greatly aided by early recognition, but cancer is a unique disease in this respect, for while it is definitely and permanently curable in its early local condition, it rapidly extends beyond this favorable stage to become a fatal disease against which neither the natural defensive mechanism of the patient nor any known methods of treatment can do more than delay to a slight extent the inevitable fatality.

It is precisely for this reason that the diagnosis of cancer in its early stages is of such vital importance, and it is in its early stages that the diagnosis of cancer is most difficult. The diagnosis of advanced cancer is all too often unmistakable, but the early case of cancer may resemble any one of many different lesions which are not cancer. Indeed, the diagnosis of early cancer is frequently beyond the abilities of even the most experienced observer, and an exploratory operation, and a frozen section diagnosis by the pathologist, are necessary before a final decision can be made.

Such conditions amply justify the pessimism of the general practitioner in regard to the cure of cancer, and even the surgeon in the local hospital to whom he sends his patients tends to share this attitude. Most of the cases he sees are far too advanced to expect a cure by operation, and even in the occasional early case his previous experience leads him to have little faith in the possibility of cure, and he is tempted either to regard his work as palliative and to content himself with an operation of less extent than is considered necessary for the radical cure of the disease, or to refer the patient to the nearest X-ray operator, regardless of the apparatus or the experience in therapeutic X-ray that may be available.

We calculate that about 12,000 cases of cancer exist at any one time in Massachusetts, and we have over 6,000 physicians registered to practise in the state. This gives us an average of only two cases of cancer a year in the practice of each physician. When we consider the almost infinite variety of locations which cancer assumes it is easy to see that the general practitioner can never be expected to make himself or keep himself expert in the difficult task of the diagnosis of early cases, or to equip himself with the necessary resources for modern treatment.

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\* Remarks at the opening of a new building at the Pondville Hospital for the Treatment of Cancer of the Department of Public Health of the Commonwealth of Massachusetts, May 20, 1930.

The physician in general practice, moreover, knows better than anyone else the mental and physical suffering, the distressing complications, and the long-continued and steadily progressing disability of the patient dying of cancer. And he is the first to appreciate the value of any such addition to his resources as is offered by the state in the Pondville Hospital. From the beginning of its service, three years ago, the Pondville Hospital has provided a service for cancer cases that is recognized, not only in Massachusetts but all over the country, as of the very highest grade, both in respect to its equipment and to its professional staff as well. With the additional resources which become available today, its position as one of the foremost cancer hospitals in the country is assured.

Under the wise direction of the Commissioner, and with the approval and support of the Governor and the Legislature, the service of this hospital has been made available, not only for the alleviation of advanced cases of cancer, but for the early diagnosis and effective treatment of early cases as well. This object is accomplished through the clinic for ambulatory cases maintained at Pondville, but it is supplemented most effectively by the organization of sixteen state-aided clinics in general hospitals distributed throughout the state. In the case of these clinics the approval of the local medical profession has wisely been made an essential requirement before any organization was attempted. As a result of this stipulation the interest and coöperation of the local medical profession in the maintenance of the efficiency of the clinic and in the reference to it of suspicious cases has been secured.

Through the permanent organization of the Department of Public Health a close coöperation has been maintained between these clinics and Pondville, and especially through the social service department the reference of suitable cases to Pondville for admission and treatment, and the follow-up of cases after discharge, back to the clinics, is facilitated.

As a result of the establishment of these institutions by the state, the advanced cancer case in Massachusetts is able to secure appropriate and effective palliative treatment, and the early case of cancer, rich or poor, can receive expert service to provide a prompt and accurate diagnosis, and can be given that treatment, whether by radiation or by surgery, which is best adapted to his individual case. Through the participation of the local medical societies throughout the state, the provision of these additional resources for the diagnosis and treatment is widely known, and a more accurate knowledge of the essential facts in regard to cancer, a greater alertness to observe suspicious symptoms and a disposition to avoid delay and to procure the immediate settlement of the question of diagnosis by reference of the patient to a special cancer clinic is already manifest. It will be indeed surprising if the benefits of these resources do not soon begin to make themselves evident by a diminishing mortality rate in place of the steadily increasing death rate for cancer which has been recorded in Massachusetts in the past twenty years.

# RELATION OF THE TECHNICIAN TO THE PATHOLOGIST

BY EDWARD B. ELLIS

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THE pathologist and the technician are, in many respects, mutually dependent. The pathologist expects, and should receive from his technician, carefully fixed, cut and stained preparations if accurate diagnoses are to be rendered promptly.

In presenting this brief note I shall recall some observations made while enjoying an association of nearly thirty years with a pathologist. If I have learned anything worth while, let me pass it on to my fellow technicians in

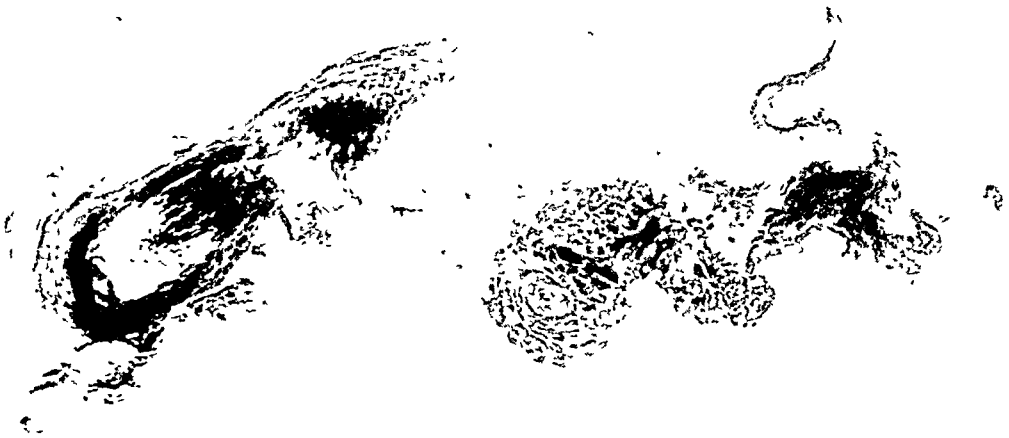


FIG. 1.—Speck of tissue less than 1 millimetre in diameter, imbedded in paraffin.  
*Diagnosis*—Squamous carcinoma.

the hope that a closer relationship may be established between the laboratory assistant and his pathologist.

Pathologic histology is an interesting branch of medicine and is evidently a difficult subject to master, hence the scarcity of competent pathologists. The technician should always bear in mind that it is his function to exert his best efforts in handling the material entrusted to his care and that the diagnosis is the pathologist's responsibility. The pathologist often experiences great difficulty in making diagnoses upon the best histological preparations. His burden should not be increased by giving him poor work. There is little excuse for such poor preparations as are often encountered today, for the modern laboratory is fully equipped to render the best service.

Some knowledge of each other's field is necessary; the pathologist must know and appreciate the technical difficulties of his assistant's work while the technician should know something of the pathological properties of the tissues he handles in order that proper differentiation may be made in the



staining of tissues. Thus he elevates himself from a mere dabbler in dyepots to a valuable technical assistant.

The technician's service will be more valuable if in his early training he

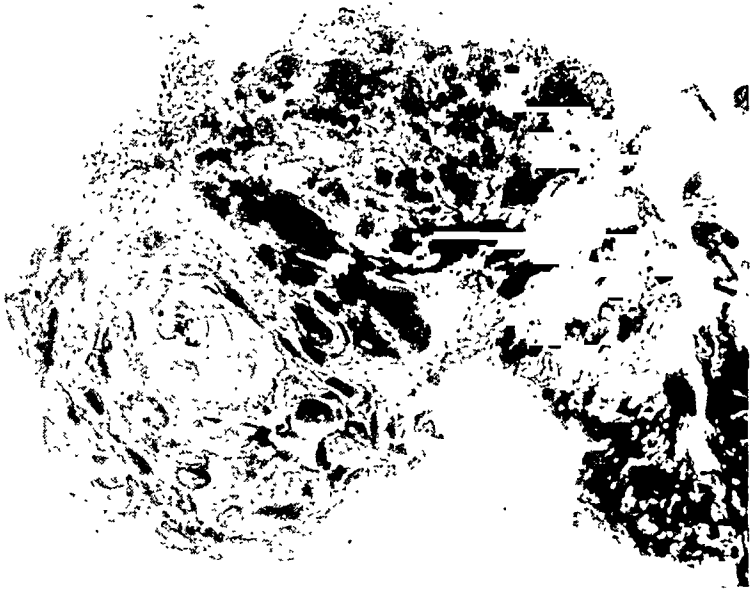


FIG. 2.—High-power magnification of Fig. 1.

secures a knowledge of normal histology. Without this he can hardly appreciate abnormal or morbid histology. Also, he will have a keener apprecia-



FIG. 3.—Biopsy. Tissue usually sent in for diagnosis, 1 to 2 millimetres in diameter.

tion of his work if he is present when the pathologist describes the gross material and selects the specimens to be prepared for diagnosis. In this way,

## THE TECHNICIAN AND THE PATHOLOGIST

if alert, he will gain some knowledge of pathology and in turn will recognize readily the proper side of a specimen to be mounted uppermost on the block for cutting. The areas of pathological importance and their relation



FIG. 4.—Large section taken through nipple of breast; embraces entire tumor mass down to muscle.

to surrounding structures having been indicated, the final section is more likely to show the essential points. He might be warned, too, of the dangers of cutting too superficially or too deeply in the block, thus missing the areas



FIG. 5.—Tumor cells aspirated from a lymph-node.

of main interest. Reputations have been endangered by poorly chosen, cut and stained preparations.

The technician should strive to master not only the procedures as out-

lined in the various textbooks of pathological technic, but should learn many of the variations, "tricks of the trade" not given in the books, but learned by practical experience. There is an urgent need for shorter methods of preparation of material in order that earlier and more accurate diagnoses may be made. These demands should appeal to the imagination of the competent technician, impelling him to invent new methods in which the time of preparation is cut down.

The extreme demands of tissue preparation are aptly demonstrated by the accompanying illustrations. In one instance (Figs. 1 and 2) we had to deal with a speck of material hardly one millimetre in diameter. Yet from this tiny bit of tissue, a positive diagnosis was obtained, demonstrating that no specimen is too small when properly selected and carried through to afford a positive opinion. Extremely large sections are now available (Fig. 4) since the method of Sir G. Lenthal Cheatle has been adopted. These show the whole picture of the disease process and its relation to the adjacent parts.

Recently we have aspirated material from suspicious areas in breast, prostate and lymph-nodes, from which we make thin slide smear preparations as for blood examination (Fig. 5). These aspirations, when properly prepared, are often the means of securing a diagnosis where a biopsy was found impractical and unsafe. Of course, the method has its limitations as have many others, but when one keeps in mind the original intent of its application, *i.e.*, the differentiation between inflammatory and neoplastic processes, its application is justified because of its simplicity and rapidity.

There are isolated instances in which the technician, by virtue of a long and close association with the pathologist, may develop considerable diagnostic ability, and in the absence of the pathologist be called upon to demonstrate the gross and microscopic material to the hospital staff, thereby increasing the value of his services. I do not desire to leave the impression that the technician, can ever function as a pathologist, but yet he may render definite aid, particularly in small hospitals where only part-time pathologists are employed.

In any work which requires the intelligent efforts of more than one person, teamwork is essential and the success attained is directly proportional to the spirit and the degree of coöperation. With these conditions fulfilled, the relationship is that of a smoothly working unit whose main object is to procure for the patient an early, accurate diagnosis.

## II

CANCER RESEARCH

- GEORGE A. SOPER, PH.D. Great Neck, L. I.  
Formerly Director of American Society for the Control of Cancer.  
"A Plea for the Encouragement of Epidemiological Research."
- DALLAS B. PHEMISTER, M.D. Chicago, Ill.  
Professor of Surgery, University of Chicago.  
"Undifferentiated Round Cell Sarcomas with Five-Year Cures."
- RICHARD MEAGHER, M.D. Boston, Mass.  
Peter Bent Brigham Hospital.  
"Concerning Intracranial Carcinomatous Metastases."
- FRED W. STEWART, M.D. New York, N. Y.  
Associate Pathologist to the Memorial Hospital.  
"An Analysis of the Lymphadenopathy Question with Special Reference to Hodgkin's Disease and Tuberculosis."
- ALFRED SCOTT WARTHIN, PH.D., M.D., LL.D. Ann Arbor, Michigan  
Professor of Pathology and Director of the Pathological Laboratories in the University of Michigan.  
"The Genetic Neoplastic Relationships of Hodgkin's Disease, Aleukemic and Leukemic Lymphoblastoma and Mycosis Fungoides."
- ELISE S. L'ESPERANCE, M.D. New York, N. Y.  
Assistant Professor of Pathology, Cornell University Medical College.  
"Studies in Hodgkin's Disease."
- BURTON T. SIMPSON, M.D. Buffalo, N. Y.  
Director of the New York State Institute for the Study of Malignant Disease.  
"Failure of Tuberculin, Karkinolysin, and Some Inorganic Compound in Therapy of Spontaneous Mouse Cancer."
- J. MAISIN, M.D. Louvain, Belgium  
Director of the Cancer Institute.  
"Susceptibility and Resistance to Tar Cancer, an Experimental Study."
- FRANK E. ADAIR, M.D. New York, N. Y.  
Attending Surgeon to Memorial Hospital.  
"Treatment of Carcinoma with Mustard Gas: A Laboratory and Clinical Study."
- FRANCIS CARTER WOOD, M.D., D.Sc. New York, N. Y.  
Director of the Institute of Cancer Research, Columbia University.  
"Animal Tumors as Therapeutic Reagents."
- OTTO WARBURG, M.D. Berlin-Dahlem, Germany  
Director of Kaiser Wilhelm Institute for Biology.  
"Mechanismus der Methylenblauatmung."

# A PLEA FOR THE ENCOURAGEMENT OF EPIDEMIOLOGICAL CANCER RESEARCH

BY GEORGE A. SOPER, PH.D.

OF NEW YORK, N. Y.

I THINK we do not realize how much we owe to epidemiological research nor appreciate what a great deal could be learned from this kind of investigation if only it could be pursued with ability and encouragement, such as are directed to other branches of cancer study.

Some of the most important facts known about cancer are of an epidemiological character. One of these is that the cancer process, or closely related phenomena, occur throughout the animal kingdom and bear a strong resemblance to abnormal growths in the plant world. Another is that some form of chronic irritation usually precedes the appearance of a cancer.

Many suppositions which are constantly taken as proved facts and serve as ground for action await confirmation or disproof by the epidemiologist. One of these is that cancer is not infectious. Another is that the death rate is increasing. Still others are the belief that the cancer death rate is higher in some cities than in others, higher in some countries than in others, higher in northern than in southern regions, and higher among some races than others. We actually know little about these matters today. There can be no doubt that many of them could be made to give up their secrets to scientific epidemiological research.

A large field of epidemiological research with distinctly practical applications lies open in the study of cancer in industry. Not much has been done to cultivate this field so far. The promise which it offers to workers in the United States is a brilliant one.

Little is known statistically about the incidence of cancer apart from the mortality, and as official mortality rates are generally inaccurate, the prevalence of cancer anywhere in the United States is largely a matter of guesswork.

The circumstances attending the onset, and, in fact, a great deal about the progress of early cancer, as distinguished from the advanced cancer which first comes to medical attention, are obscure and not likely soon to be made clear by chance observations such as have thus far contributed most of the information which exists on this subject.

Epidemiological research of the right sort is capable of clearing up many of these points in the future as partial investigations and pronouncements of the wrong kind have done so much to obscure the truth about them in the past.

Statisticians, often with no knowledge or concern as to the accuracy of their fundamental data, but interested chiefly in compiling tables, have pub-

lished figures and based opinions on them which are seriously misleading as to cancer mortality. One country has been compared with another, one region with another, and cities have been classified according to these assumptions of cancer mortality. The effect is to obscure the truth about cancer.

Under the best circumstances which now obtain, the official general cancer mortality statistics which are compiled by our cities and states are seriously in error and in the hope of emphasizing the need of giving proper epidemiological attention to this topic a few words about these rates may be appropriate.

Nearly all the states publish rates which are known to those who are acquainted with more correct methods as "crude" rates. They are compiled by multiplying the number of cancer deaths reported during the year by 100,000 and dividing the product by the estimated mid-year population. Forty-two of the forty-eight states, including the cities within them, and twenty-one cities in states whose vital statistics are too incorrect for use, are included in what the United States Government calls the Registration Area in the continental part of the United States. The registration area is not fixed; it has increased from time to time since 1880, when it was established. In 1927, it included 91.3 per cent. of the population, or 108,327,000 persons.

The United States Census Bureau, which regularly publishes the mortality rates for the registration area and has given a great deal of careful attention to the subject of cancer, has recalculated the cancer death rates and in doing so has made certain corrections which show that the crude rates as published by the cities and states are misleading. It has made allowance for inequalities in the proportion of males and females in the population and for the number of persons present in each age group, it being known that cancer exacts a higher toll among women than men and among old people than young ones. The resulting tables of "adjusted" rates, as they are called, show much smaller differences among the cities and states than the crude rates indicate.

Thus, Vermont's rate falls from 131.7 to 89.6 and Albany's from 182.4 to 143.1, while Louisiana's rises from 67.9 to 85.6 and Detroit's from 78.4 to 108.5 per 100,000 population. Changes were made in the official rates of practically all the states and cities.

The highest and lowest crude rates in 1927 were, for the states, Maine, 137.2, and South Carolina, 41.2. The highest and lowest adjusted rates were, New York, 114.5, and South Carolina, 57.0. In the first case the difference was 96.0 and in the second, 57.5.

Smaller differences between the maximum and minimum rates also were found among the cities when the adjusted rates were compared than when the crude rates were considered. For example, the crude rate for Albany was 182.4, and for Norfolk, 55.2, whereas the adjusted rate for Albany was 143.1 and for Norfolk, 68.7. The greatest difference between the crude rates was 127.2 and between the adjusted rates, 74.4.

Other tables of mortality rates have been prepared by the Census Bureau in which allowance has first been made for the actual residence of the deceased before the adjusted rates have been calculated, with the object of allowing for the fact that a certain number of patients go to some other city or place for medical, hospital or institutional care and die away from home. These "refined" rates, as they are called, still further alter the order and range of the inequalities among the states and cities and show that the adjusted rates do not afford information from which correct inferences may be drawn, as to the relative mortality from cancer.

Among the states, the highest refined rate in 1927 was, for New York, 113.2, and the lowest, for North Carolina, 63.5. The difference between these extremes was 49.7. Among the cities the highest refined rate was for New York, 136.0, and the lowest, for Norfolk, 56.3. The difference was 79.7.

The refined rates show that the crude and adjusted rates are misleading, but it is probable that they are not right themselves. Nobody knows how near the truth they are. Is it likely that the true cancer death rate is 78 per cent. higher in New York State than it is in North Carolina, or 141 per cent. higher in New York City than in Norfolk? If so many more people are dying of cancer in New York in proportion to the population than are dying in the southern cities, it is of the utmost importance to learn why. If this difference is only apparent and not real, the errors should be discovered and removed. Apparently there is a considerable difference even if it has not been measured exactly. What is it due to? Would it not be desirable to see what a well-trained epidemiologist could find out about this matter?

Any rate is correct only in so far as the fundamental data upon which it rests are correct and if the underlying information as to the cause of death, residence, age or sex is not exact or the age or sex distribution of the population is not properly determined no calculation will yield a correct result. It would seem that all the errors inherent in the crude rates had not been eliminated in the refined rates. This is no reflection upon the Census Bureau or upon any person or body. The Bureau is deserving of the highest praise for the numerous studies it has made of cancer statistics. Its work surpasses that of most countries. We are simply faced with a situation in which scientific epidemiological work is called for. The study needs to be carried into the field.

Let us consider for a moment the completeness and accuracy of the original returns which go to make up the cancer statistics of our cities, states, and the general government.

Aside from the omission of a death certificate altogether, there are three principal factors which tend to make the registration of a death from cancer inaccurate: mistakes in diagnosis, mistakes in making out the death certificate, and attempts to hide cancer as the cause of death out of consideration for the feelings of the family of the deceased. It is a matter of opinion



how far these factors operate and the extent to which they influence the returns. Some persons think the reports are fuller and more correct in certain parts of the United States than they are in others. It seems futile to argue about it. The question ought to be settled through epidemiological research.

As to diagnosis, one need go no further perhaps at the present moment than to recall the fact that cancer is often mistaken for other conditions and that these may be set down as the cause of death. Cancer may fail of recognition even at the time of death in large, well-equipped hospitals where every facility exists for diagnosis. In large cities the mistakes have been found through autopsy to run as high as 30 or 40 per cent. Through the country, and especially in private practice and where the deceased has had little or no medical attention, the mistakes must be much more numerous.

How far, then, official cancer death rates are to be depended on, where they are in error, and how the mistakes can be corrected should be determined by epidemiological study.

So much confusion appears to exist between the terms statistical and epidemiological research that this brief contribution will be closed with a few words intended to point out the difference between these two methods of investigation as they appear to me.

Statistical research is essentially mathematical. Collections of numerical data are made and arranged in various ways. These may be calculations of averages, percentages, trends, norms, probable errors, and so on. Tables and curves illustrate these results. Interest centres on the information which can be extracted from a study of the figures. The gathering of the data receives less attention. Statistical research is essentially a closet study.

Epidemiological research may or may not make use of statistics. Much attention is given to the collection of the data. The investigator must have a considerable knowledge of the disease investigated. He gathers detailed information on a great many topics and as carefully weighs it. His is usually, but not invariably, a field study. He makes use of whatever method of investigation promises to give him reliable results. His aim is to help point the way to prevention and cure. He is vitally interested, therefore, in the thing studied.

There are two distinct kinds of epidemiological investigation which should be noted: extensive and intensive. Extensive work usually employs large arrays of figures and seeks to arrive at conclusions through the study of readily recognizable and measurable conditions of wide application. Intensive epidemiological research may be carried on with a very few cases. It is the penetrating character of the investigation which is directed at a small number of characteristic cases which brings out the desired information in intensive epidemiological work.

Both are needed in cancer research. I believe there is no other field of investigation which, with proper encouragement, is capable of producing results of comparable value.

# UNDIFFERENTIATED ROUND-CELL SARCOMAS

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FROM THE DEPARTMENT OF SURGERY OF THE UNIVERSITY OF CHICAGO

For many years the usual teaching in connection with malignant tumors was that the less differentiated the cell, the more malignant the tumor, the earlier it gives rise to metastases, and the worse the prognosis. It has been held particularly for carcinomas, and Broders<sup>1</sup> has classified them into four types according to their morphology which correspond roughly to their degree of malignancy. While this may be true for tumors in general; all four assumptions merit criticism for particular types of tumors. Thus, Borst<sup>2</sup> points out that certain highly differentiated tumors presenting a histological picture approaching mature tissue may behave like malignant neoplasms. Sarcoma presents exceptions to the rule oftener than carcinoma and there is perhaps no better example than is offered by the undifferentiated round-cell sarcoma met with most frequently in connection with the bones and the connective tissues of the soft parts of the extremities. Five cases which occurred in adults came under my care during the period of 1919-1925, and all five are alive and free from signs of recurrence at the time of writing, July 1, 1930; one for ten years and nine months; one for eight years and three months; one for seven years and two months; one for six years and four months; and one for four years and eight months. Exceptions to one or more of the rules enumerated were shown by all five tumors. Four of them were entirely undifferentiated consisting of round or polyhedral cells and almost entirely devoid of stroma except for the blood-vessels. One tumor showed organoid character in that it possessed a connective-tissue stroma in places. Two of the tumors increased in size rapidly, while two increased slowly after the detection of the initial swelling. All of the tumors were treated before they were of sufficient size to produce cachexia, although one of them had reached dimensions that were compatible with it. In no instance was there evidence of metastases nor have metastases developed since treatment was initiated. The prognosis in this type of case has been greatly modified by the use of irradiation therapy, since the group ranks among the most radiosensitive of tumors. However, the largest tumor of the group was treated by amputation, which emphasizes particularly the fact that metastases may be absent although the disease is advanced. The therapy employed in these cases was extremely varied. In one case it consisted of amputation only; in one case it consisted only of irradiation by means of radium and X-rays; while in two cases it consisted of X-ray irradiation followed soon by excision and radium implantation with subsequent X-ray irradiation. In one case the tumor disappeared under X-ray irradiation, after which the bone in which it had developed was excised and further X-ray irradiation

was employed. It is interesting in view of the fear entertained by many, of spreading metastases through operative interference, that biopsy was performed in four cases; that in one case there was an extensive regional excision eighteen months previously followed by a prompt recurrence; that in two cases there was apparently incomplete local removal after pre-operative X-ray irradiation; and that in one case there was a pathological fracture of the involved bone one month before the patient was seen and that a biopsy was performed one week before the beginning of the irradiation.



FIG. 1.—Case I. Saggital section of scapula and tumor. Infrapinatus muscle (a), skin (b).

CASE I.—Male, aged twenty-nine, was seen because of a large swelling of the dorsum of the right scapula which had developed during the previous seven months. At first the swelling was symptomless, but recently it had produced some pain and considerable limitation of motion in the shoulder. No loss in weight or strength. Examination showed a large, firm, soft, oval swelling involving the entire posterior scapular region and limiting elevation of the arm. General condition of patient excellent. No enlargement of axillary or cervical glands. Röntgenogram of right shoulder negative for bone change. Röntgenogram of chest was negative for lung metastases.

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*Operation.*—Intrathoracoscapular amputation. Pathological examination revealed a grayish, soft, oval tumor which occupied the entire posterior scapular region (Fig. 1). It came into contact with the bone above and was separated from it below by the infraspinatus muscle. The tumor protruded forward between the glenoid and coracoid process making an egg-sized mass extending into the axilla. It produced little bony erosion where it was in contact with the upper portion of the bone. The muscles of the region were extensively invaded by the tumor and at the level of the spine of the scapula it infiltrated the deeper portions of the skin.

Microscopic examination showed the entire tumor to be extremely cellular. It was

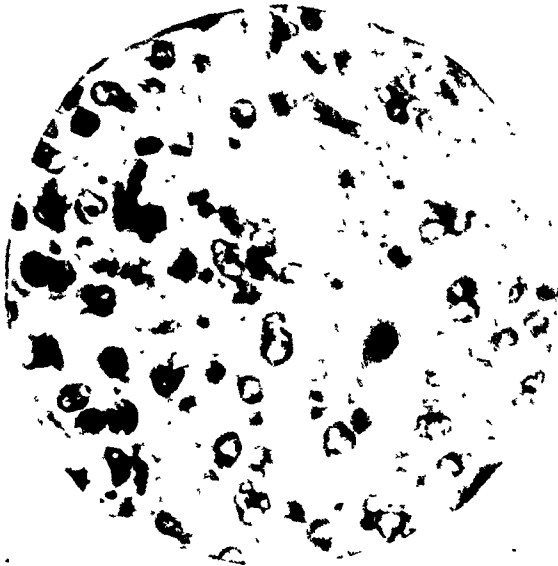


FIG. 2.—Case I. Magnification 625 diameters.



FIG. 3.—Case II. Magnification 300 diameters.

composed largely of medium-sized round cells with more or less irregularly shaped nuclei. Hyperchromatic nuclei were common but mitotic figures were scarce (Fig. 2). There was practically no intercellular substance present aside from blood-vessels. Sections from a deeper portion of the tumor showed much necrosis.

*Diagnosis.*—Paraosteal undifferentiated round-cell sarcoma.

*Post-operative Course.*—There was an uneventful recovery from operation and the patient has remained entirely well and free from signs of recurrence up to now, ten years and nine months after operation.

**CASE II.**—Female, aged forty-four. Two years and three months before examination patient had noticed a soft swelling on the lateral aspect of the right arm above the external condyle. It increased slowly in size and eighteen months later was excised and found to be a sarcoma. A small amount of X-ray treatment was given but the lesion recurred and had gradually increased in size. Examination revealed nothing abnormal aside from the right arm. There was an oval mass 12 centimetres long by 6 centimetres wide occupying the anterior and lateral aspect of the lower portion of the right upper arm. It was soft, fixed, and extended from subcutaneous tissue to the bone. A röntgenogram of the humerus was negative for bone changes and there were no signs of metastases in röntgenograms of the chest.

A pre-operative massive deep X-ray treatment was given with a 200,000-volt current delivering  $4/5$  of an erythema dose. One week later the tumor was excised locally. It extended from subcutaneous tissue to bone and was soft and grayish in color, infiltrating the muscles and surrounding the radial nerve which was excised. Tumor was broken into at operation and was curetted off of the front of the humerus, the removal being evidently incomplete. Eight needles containing  $12\frac{1}{2}$  milligrams each of radium were implanted in the field, four of them in contact with the supracondylar portion of the humerus in front. They were removed in ten hours.

Microscopic examination of the excised tumor showed it to consist of large round cells

which were well preserved in the narrow peripheral portion but which were extensively necrotic in the central portion. There was practically no stroma throughout the tumor (Fig. 3). Irregular mitoses and hyperchromatic nuclei were occasionally to be seen.

*Post-operative Course.*—The wound healed with a slight serous discharge which persisted for two weeks. Four months and eight months later the patient received  $\frac{1}{2}$  of an erythema dose of deep X-ray therapy to the region. Sixteen months later a mild acute inflammation developed in the field, leading to the formation of a discharging sinus that healed after two weeks. The patient has since remained well and there have been no signs of local recurrence or metastases up to the present time, eight years and three months after operation.

*Radium Necrosis of Humerus.*—A very interesting change was that produced by the radium which came into contact with the front of the humerus. It was left *in situ* long enough to produce an extensive area of necrosis. The dead bone subsequently underwent sequestration but it was at an extremely slow rate as compared with the sequestration



FIG. 4.—Case II. Sixteen months after radium exposure at (x). No sign of absorption or sequestration of bone killed by radium.



FIG. 5.—Case II. Three years and ten months after radium application, showing beginning absorption of radium. Dead bone (x).



FIG. 6.—Case II. Sequestration of dead bone (x) complete eight years and two months after radium exposure.

of bone that is killed as a result of pyogenic infection. A röntgenogram taken sixteen months after operation and radium implantation revealed no change in the humerus at the seat of radium exposure (Fig. 4). A röntgenogram three years and ten months after the operation revealed evidence of irregular absorption of bone in the anterior supracondylar region, but no sequestration (Fig. 5). A röntgenogram taken five years and ten months after operation showed further absorption and sequestration almost complete with compensatory new bone formation along the posterior surface of the humerus at that level. A röntgenogram taken eight years and two months after operation revealed complete sequestration of the dead bone which had become slightly displaced from its bed anteriorly (Fig. 6).

The extremely slow rate of sequestration and absorption of the dead bone was due undoubtedly to the fact that the surrounding tissues which had to do the absorbing were radium burnt and consequently reacted very sluggishly. The presence of a slight, low-grade infection probably had something to do with the fact that the dead bone was

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sequestered rather than replaced by creeping substitution as was found to be the case in experiments<sup>3</sup> when bone killed aseptically by radium functions in the support of the extremity and as was observed in Case V of this series.

CASE III.—Female, aged thirty, complained of a gradually increasing swelling of the right deltoid region of six months' duration. Two months previously it had been biopsied and pronounced sarcoma. The swelling had gradually increased in size but there had been no local or general disturbance. Eleven years previously the head of the right humerus had been resected because of a chronic arthritis of the shoulder, the nature of which was unknown. Since then the shoulder had been symptom free, but was markedly restricted in motion. Physical examination was negative aside from the right shoulder region. There was a large, tense, soft, oval swelling in the region of the right deltoid muscle which measured about 12 centimetres in its longitudinal axis. Marked fixation of shoulder-joint. A röntgenogram revealed absence of head of humerus but no sign of erosion of the side of the shaft in the region of the soft-parts swelling. A second biopsy was performed which revealed an extremely cellular, small, round-celled tumor that contained almost no stroma and a few blood-vessels (Fig. 7). There were many polyhedral cells and a fair number of mitotic figures.

*Diagnosis.*—Paraosteal undifferentiated round-cell sarcoma. Two massive X-ray treatments were given one week apart, one front and one back, comprising an erythema dose. Tumor began to slough out through the biopsy incision. Two weeks later the tumor was excised locally. It lay beneath and invaded the deltoid and came into contact with the bone. It was cut into and scooped out, after which the walls were cut away. Apparently an incomplete removal was accomplished. Twelve needles each containing 12½ milligrams of radium were

implanted in the field and left for twelve hours. One month subsequently she received ¾ of an erythema dose of massive deep X-rays. This was repeated three weeks later. The wound was moderately infected but gradually healed in the course of two months. The patient has remained in good health and free from evidences of a recurrence up to now, six years and four months after the operation. Although radium came into contact with bone, so far there has been no sign of sequestration of the dead bone.

CASE IV.—Male, aged thirty-three, sustained a fracture of the outer third of the right clavicle as a result of lifting thirty-seven days before examination. The arm had been kept bandaged to the side but slight pain had continued at the seat of fracture and a swelling had appeared gradually. Examination revealed a firm, oval, soft swelling, centring at the junction of the outer and middle thirds of the clavicle, which extended both above and below the bone for a distance of about 7 centimetres. A false point of motion could be elicited in the clavicle at this point. A röntgenogram revealed an irregular area of destruction extending over a distance of 4 centimetres in the clavicle about the junction of the outer and middle thirds with a fracture through it and downward displacement of the outer fragment. The shadow of an oval, soft-parts tumor could be seen about it. Biopsy revealed a grayish, soft tumor about 2 centimetres thick covering the bone. Microscopic examination showed the tissue to be composed of densely packed round cells and of a smaller number of polyhedral cells of uniform size. There were numerous capillaries throughout the tumor and but little necrosis. There were many hyperchromatic nuclei and very few mitotic figures. No bone or other type of stroma

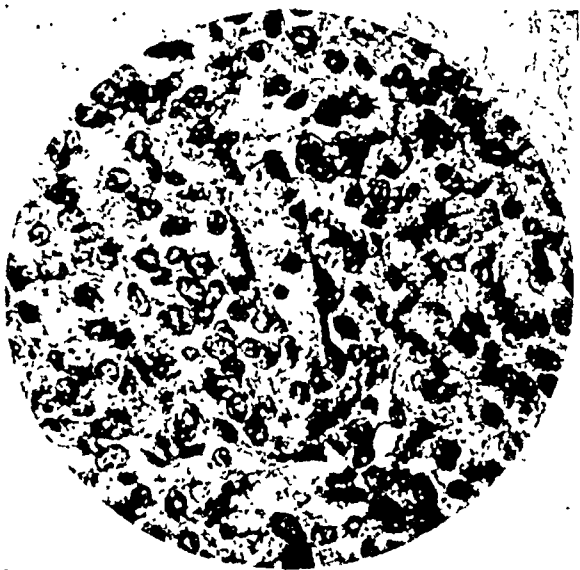


FIG. 7.—Case III. Paraosteal sarcoma of subdeltoid region.

*Diagnosis.*—Undifferentiated round-cell sarcoma of the clavicle with pathological fracture.

Röntgen-ray therapy was started one week later. A series of eight regional treatments was given at the rate of three per week using 140,000 kilovolts and delivering altogether  $5/7$  of an erythema dose. Two months later two treatments of massive deep X-ray were given front and back at two-week intervals delivering an erythema dose. Under treatment the mass gradually disappeared and the fracture became firm although röntgenologically an irregular, broad line of reduced density at the seat of the intermediary callus could still be seen. Because of the possibility that tumor might be retained within the bone the outer  $4/5$  of the clavicle including soft parts about the old region of tumor was excised four and a half months after the biopsy. No tumor was seen grossly about

the seat of fracture at which point there was an irregular, spindle-shaped swelling. Longitudinal section of the bone revealed a broad, irregular, cartilaginous intermediary callus at the seat of fracture and grayish necrotic tissue in the marrow cavity of the mesial fragment (Fig. 8). Microscopic sections of the entire extent of the previously involved clavicle revealed signs of an old healing fracture but no traces of tumor could be found. There was some necrotic bone and cancellous débris in the end of the mesial fragment. Sections of the surrounding soft parts revealed scar tissue and muscle but no traces of tumor. The patient has remained well and free from signs of recurrence during the four years and four months since the operation or four years and eight months since Röntgen-ray treatment was started.

In this case both the pathological fracture and the biopsy might be regarded as factors that would predispose to the development of metastases and still none have so far made their appearance.

CASE V.—Female, aged fifty-six, complained of pain in the left sciatic region for nine months and a limp and swelling in the region of the left ischium for five months. Examination revealed an elderly woman in good general health. There was a soft mass in the region of the body of the left ischium, bulging both laterally and mesially and approximately 10 centimetres in diameter. Examination otherwise essentially negative. A röntgenogram revealed extensive, irregular reduction in density in body and ramus of the left ischium. Biopsy revealed a firm, grayish tumor mass. Microscopically it consisted of masses of small round cells which in regions were separated by irregular bands of immature connective tissue giving the tumor an organoid appearance. There were numerous hyperchromatic nuclei among the round cells with few mitotic figures. No mitoses were seen in the connective tissue portions. Blood-vessels were fairly numerous throughout the section. A diagnosis of undifferentiated round-cell sarcoma of the ischium was made and the lesion was treated entirely by irradiation. Eight needles containing each  $12\frac{1}{2}$  milligrams of radium were introduced by means of spikes and left for thirteen hours delivering 1300 milligram hours. The procedure was repeated in four weeks. Following this four series of eight regional X-ray treatments were given with an interval of two months between  $5/7$  of an erythema dose being given during each series. The tumor and symptoms disappeared under treatment and subsequent radiograms showed re-ossification of the ischium. She has remained free



FIG. 8.—Case IV. Section of excised clavicle showing disappearance of tumor and the cartilaginous intermediary callus of pathological fracture.

and subsequent radiograms showed re-ossification of the ischium. She has remained free

## UNDIFFERENTIATED ROUND-CELL SARCOMAS

from physical and X-ray evidences of recurrence for seven years and two months since treatment. There have been occasional pains in the hip from time to time and the patient was complaining when last examined but radiograms have shown no evidence of recurrent destruction of bone and no signs of pulmonary metastases. The bone killed by radium has not been sequestered. Her general health is good. Because of these symptoms there is more reason to doubt a permanent cure in this case than in the others.

The degree of differentiation of these tumors was so slight that it was impossible to state the type of tissue to which they belonged. Some would no doubt classify them as Ewing's endothelioma, but three tumors arose outside of bone in locations where endothelioma rarely develops. It is difficult to estimate the value of the local excision employed in the three cases with irradiation therapy. In Cases II and III where it was preceded and followed by irradiation, large amounts of tumor were removed, and only scattered bits left behind; consequently the body had less tumor to resist and irradiation less to overcome and there can be little doubt that this creates an advantageous situation. Failure to find tumor cells histologically in the excised clavicle in Case IV is no proof that there might not have been a recurrence had it been let alone.

### SUMMARY

Cures lasting from four and two-thirds to ten and three-fourths years have been obtained in five cases of undifferentiated round-cell sarcomas, two of which began in bone and three in the connective tissues about bone. Biopsy performed in four cases, a pathological fracture in one and a previous incomplete operation in one did not lead to metastases. This experience favors the view that biopsy is not a dangerous procedure. One tumor was treated by irradiation only, one by amputation, and three by both irradiation and local excision. Several years were required in case 2 for sequestration of the bone killed by radium used in the treatment due to the fact that the adjacent tissues which produced the absorption were radium burnt.

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# INTRACRANIAL CARCINOMATOUS METASTASES

WITH NOTE ON RELATION OF CARCINOMA AND TUBERCLE

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IN ANY large series of intracranial tumors there is certain to be found a definite percentage of metastatic carcinomas. Many of these are readily predictable following careful examination of the breast, and of late years the more routine use of chest plates has shown the true place of the lung as an unsuspected and often otherwise undemonstrable source of primary cancer. The infrequency of coëxisting multiple primary intracranial tumors of different types, there being only four such examples observed in our series, makes the appearance of bilateral or combined cerebral and cerebellar signs of great diagnostic significance. The occasional systemic manifestations, the rapid onset of intracranial signs, and the speedy downward course which many of these patients pursue frequently offer a clue to a presumptive diagnosis in spite of inability to demonstrate a primary site of malignancy. There remain, however, a certain number in which the pre-operative diagnosis is missed, and it is in the hope of further correlating our known observations that the following statistics are offered.

In a series of 1,850 verified intracranial tumors to May 10, 1930, fifty-seven are metastatic, representing 3 per cent. of the total. Of these forty-four are carcinomas, four are hypernephromas, and nine are sarcomas. This does not, of course, represent the true relation of metastatic tumors to tumors as a whole, because the prognosis of these patients, generally speaking, is so unfavorable that they are rarely deemed fit subjects for operation, and consequently many of them remain in the unverified group.

Grant,<sup>1</sup> in a previous report from this clinic, summarized the records of the various intracranial metastases to March, 1926. In the present study particular attention will be given to the carcinomas.

The primary site of the forty examples of carcinoma in the Brigham Hospital series is shown in the following table:

| Primary focus               | No. of cases | Per cent. |
|-----------------------------|--------------|-----------|
| Breast .....                | 10           | 25.0      |
| Lung .....                  | 14           | 35.0      |
| Mouth and sinuses .....     | 2            | 5.0       |
| Liver and intestines .....  | 2            | 5.0       |
| Generative organs .....     | 1            | 2.5       |
| Kidney .....                | 1            | 2.5       |
| Primary focus unknown ..... | 10           | 25.0      |

As may be seen from the above, lung and breast comprise 60 per cent. of the series, and are the only tumors in sufficient numbers to make general

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estimations of value. Fried and Buckley<sup>2</sup> have stressed the insidious course of primary lung cancers with suddenly developing intracranial signs, and it is impossible to judge the time of onset of the primary malignancy.

Breast carcinomas, however, since they are so frequently operated upon, lend themselves to more detailed records, and in the following table a summary of the ten cases of intracranial metastases in which the primary focus occurred in the breast is given.

| Case        | Age | Period from breast operation to onset of intracranial symptoms | Period from presence of lump to onset of intracranial symptoms | Survival period after intracranial operation | Survival period after onset of intracranial symptoms |
|-------------|-----|--|--|--|--|
| 1.....      | 61  | 6 yrs. 4 mos.  | 7 yrs. 10 mos.   | (No operation)                               | 8½ mos.  |
| 2.....      | 42  | 6 mos.   | .....  | (No operation)                               | 4 mos.   |
| 3.....      | 65  | 11 yrs. 9 mos.   | .....  | (No operation)                               | 3½ mos.  |
| 4.....      | 50  | 3 mos.   | .....  | 3 mos.                                       | 8 mos.   |
| 5.....      | 53  | 2 yrs. 6 mos.  | .....  | 1 day  | 6 mos.   |
| 6.....      | 49  | .....  | 1 yr. 10 mos.  | 2 weeks                                      | 3½ mos.  |
| 7.....      | 59  | 6 yrs. 2 mos.  | .....  | 3 weeks                                      | 9 mos.   |
| 8.....      | 30  | 3 yrs. 4 mos.  | 3 yrs. 11 mos.   | 5 mos.                                       | 9 mos.   |
| 9.....      | 50  | .....  | (Duration not noted)   | 1 mo.  | 7 mos.   |
| 10.....     | 52  | 1 yr. 1 mo.  | .....  | Living                                       | Living   |
| Average.... | 51  | 3 yrs. 10 mos.   | .....  | 6 weeks                                      | 6 months   |

In this group, the ages vary from thirty to sixty-five years, the average being fifty-one years. The longest survival period after operation is five months, the average being six weeks, while the longest survival period after the onset of intracranial symptoms is nine months. The time interval between the breast operation and the appearance of the intracranial symptoms varies widely, the shortest period being three months, and the longest nearly twelve years, an average of over three and a half years. Since tissue from the primary tumor is usually unavailable, it is impossible to hazard more than a guess as to the rôle the type or extent of the tumor plays in determining the probability of intracranial metastasis. From the diagnostic point of view no positive stand can be taken on mere time interval alone even after considering the age of the patient and histological grade of malignancy of the primary lesion. Moreover the so-called typical clinical history of very rapid progress of an intracranial lesion, often with an accompanying psychosis, cannot always be relied upon, even in cases of established breast cancer. As an example of this the following case is cited.

CASE I.—P. B. B. H. Surg. No. 35806. Admitted January 9, 1930. Woman, L. M. N., forty-eight years of age, complaining of severe headache of three months' duration. *Family history* unremarkable.

*Past history.*—Twelve years ago she began to have fainting spells which lasted from a few minutes to almost an hour and were unaccompanied by convulsions. Her second attack came on one year after the first, and over a period of four years she had irregularly recurrent seizures with no increase in frequency or severity. At this time she was subjected to an appendectomy, the uterus was suspended and a small ovarian cyst was

removed. Within a year of this operation her attacks ceased save for a single lapse of consciousness five years ago. She had no further complaints and believed herself in excellent health.

Two years ago, in January, 1928, she noted a hard painless lump in the upper inner quadrant of the left breast. This gave her no concern but its persistence caused her to seek examination a little more than a year later and the mass was noted as being 4 centimetres in diameter, slightly adherent to the skin and with no evidence of axillary or supraclavicular involvement. The opposite breast was normal. On June 6, 1929, eight months prior to entry, a radical amputation was performed and although grossly no axillary extension was demonstrable, section showed a carcinoma simplex of scirrhus type, Grade II, with metastases to lymph-node. Healing was good and recovery rapid.

*Present illness.*—Four and a half months before entry (two and a half months after her radical breast operation), she began suddenly to have severe occipital and vertical headaches. Patient immediately thought of her eyes, but altered lenses gave no relief. The headaches continued with frequent remissions up to the time of admission and the last two months were definitely milder until one week before entry, at which time she had a very severe headache with nausea and vomiting. She had had no peripheral motor or sensory symptoms and no visual disturbances.

*Neurological examination* showed a very slight secondary atrophy of left nerve head without choking and no further signs whatsoever.

*X-ray findings.*—Skull plates disclosed a mass 9 by 9 by 7 centimetres in the right temporal region which was of markedly increased density. There were mild skull changes of increased pressure. The röntgenologist's impression was that it was a meningioma. The lungs were noted as clear.

*Operation.*—In view of the positive X-ray findings, operation was performed in two stages on January 31, 1930, and February 1, 1930, with removal of a meningioma rich in calcium. As removal progressed, the last remaining attachment of the mass contained the main branch of the middle cerebral artery, injury of which caused a fatal hæmorrhage. Subsequent section of the brain failed to reveal any sign of metastatic carcinoma.

*Comment.*—The history of sudden onset of terrific headaches, nausea and vomiting in a woman of forty-eight, who seven months before entry had a radical breast amputation for a scirrhus carcinoma of rather high malignancy with axillary metastases, strongly suggested intracranial metastasis until the routine X-ray examination disclosed a partially calcified meningioma. The case well illustrates the difficulty that may confront the surgeon in making up his mind from the clinical history alone as to the nature of the lesion he expects to find.

If this difficulty exists in the case of patients with obvious breast tumor or with the scar of a breast amputation to suggest the probability of the nature of the intracranial growth, the diagnosis of a primary carcinoma of the lung is still more obscure, the primary lesion having been recognized in only four of the fourteen cases, in contrast to 90 per cent. of correct pre-operative diagnoses of metastases from the breast.

It is the usual clinical practice to consider a syndrome of a single etiology, and when two supposedly antagonistic lesions, both capable of producing the same intracranial signs, are found in the same individual, one is faced with a diagnostic problem in which the opinion of various observers must be evaluated. Just such a situation existed in the following case.

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CASE II.—P. B. B. H. Surg. No. 35063. Admitted October 18, 1929, woman, M. G., aged thirty, with complaint of occipital headaches, failing vision, nausea and vomiting of four months' duration.

*Family history.*—Direct and prolonged exposure to active tuberculosis among members of her immediate family, four of whom succumbed to pulmonary tuberculosis and with whom she was associated intimately from childhood.

*Past history.*—In 1903, at the age of four years, she had tuberculosis of the right

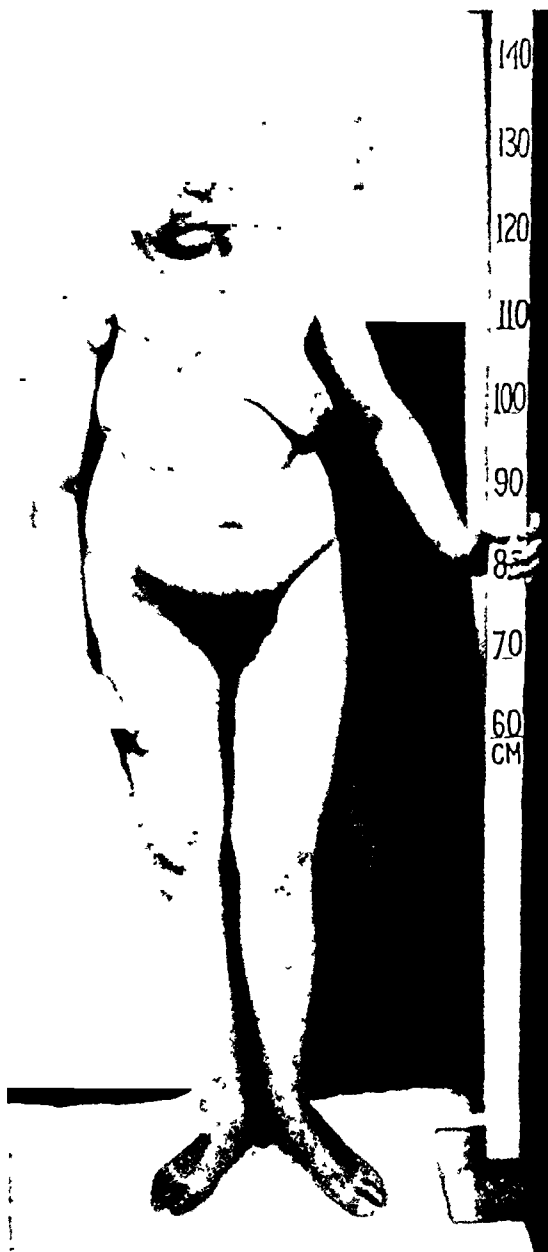


FIG. 1.—Case II. Showing scar of radical breast amputation and deformity of hip.

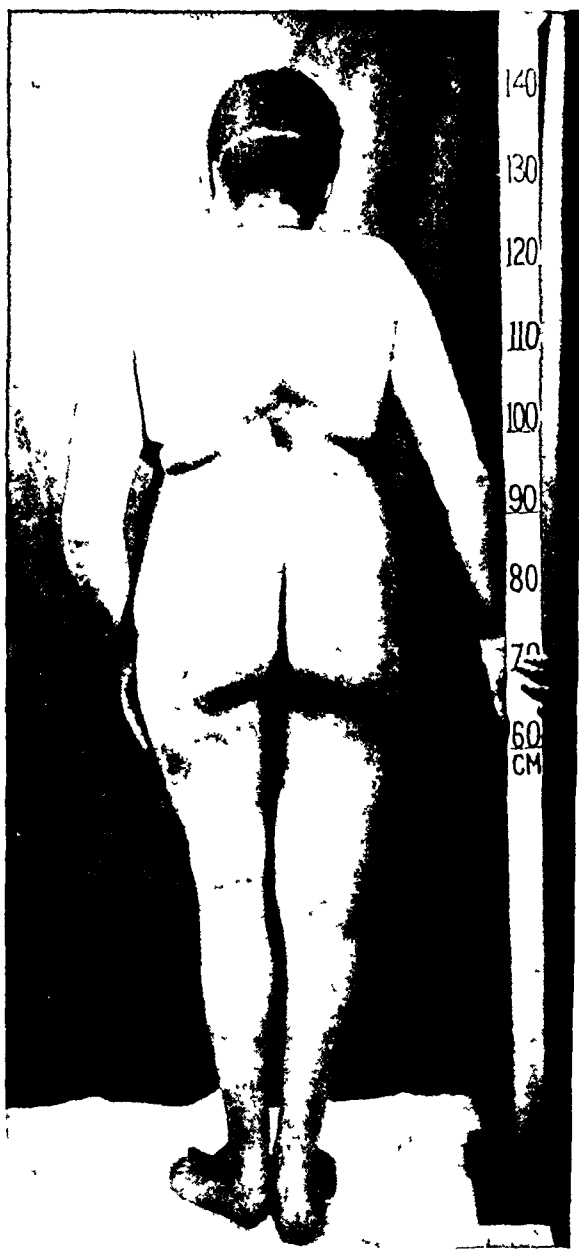


FIG. 2.—Case II. Showing marked spinal deformity. Note scars of suboccipital exploration and spinal fusion operation.

ankle with discharging sinuses, which after treatment for three years at the Children's Hospital finally healed satisfactorily.

In 1905 she began having symptoms associated with the left hip-joint, and a year later was admitted to the wards of the Children's Hospital for treatment of tuberculosis of this joint. She did fairly well under observation for the next two years until a tuberculous abscess developed at the end of that period.

In 1913, at the age of fourteen, she was admitted to the Carney Hospital with tuber-

culosis of the spine. An Albee spine operation was performed with fusion of the fourth to tenth dorsal processes.

Except for a story of "influenzal pneumonia" in 1919, the history during the next thirteen years was quite uneventful.

In 1926, at the age of twenty-seven, the patient was again admitted to the Carney Hospital, with complaint of a lump in the right breast of seven months' duration. February 18, 1926, a radical amputation of the breast was performed, with removal of a

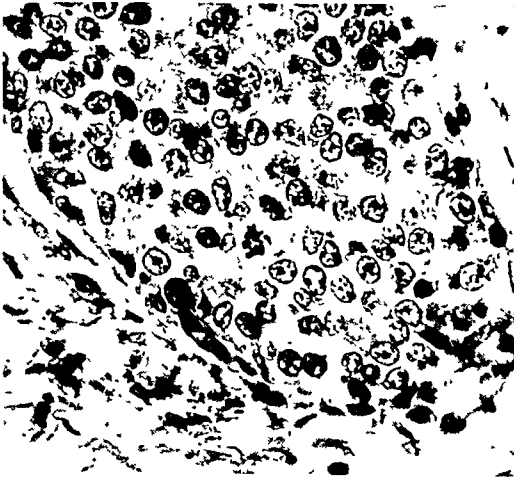


FIG. 3.—Case II. Characteristic field of scirrhous carcinoma simplex of breast. (Hematoxylin eosin stain  $\times 600$ .)

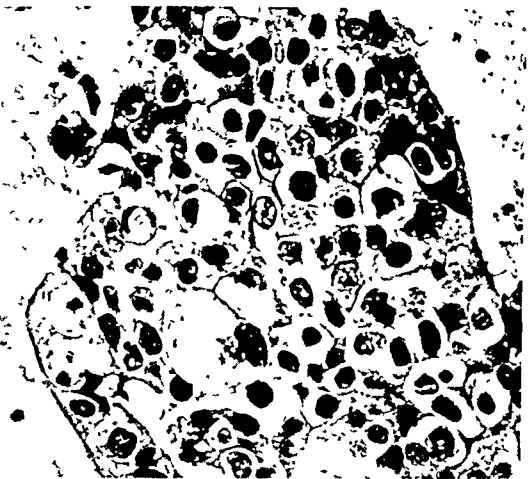


FIG. 4.—Case II. Intracerebellar metastasis of the same tumor shown in Fig. 3. The cells are much larger and there are numerous mitoses. (Hematoxylin eosin stain  $\times 600$ .)

very hard nodular carcinoma in the left upper quadrant, which was adherent to the skin. There were no masses in either axilla except for one small gland in which no evidence of malignancy was found.

*Present illness.*—For four months severe occipital headaches associated with stiffness of the neck, nausea and vomiting; diminution in vision; irregularity of menses. For three months diplopia, persistent until two weeks before entry. Four weeks ago the patient suffered two seizures in which she lost consciousness and bit her tongue, though no clonic movements were observed. On both occasions she complained of transitory numbness of the left hand preceding the attack.

*Physical examination.*—The signs of her healed tuberculosis were a partially ankylosed right ankle and left hip, and immobilization and deformity of the dorsal spines with marked kyphosis (Figs. 1 and 2). The chest was free of signs, but X-rays showed evidence of old healed pulmonary tuberculosis. There was no evidence of local recurrence in the skin of breast or axilla.

Neurological examination revealed bilateral choked discs  $4\frac{1}{2}$  D. right and 3 D. left. Deep reflexes were exaggerated on both sides.

*Pre-operative diagnosis.*—Cerebellar tumor. The localizing symptoms were insignificant except for the history of suboccipital headaches. Owing to rigidity of the leg and dorsal kyphosis, gait and station were difficult to test. Although a lesion of the posterior fossa was suspected, in view of the story of left-sided attacks a preliminary ventriculography was made, which disclosed an internal hydrocephalus.

*Operation.*—October 24, 1929. Suboccipital exploration with disclosure of what was regarded as a patch of tuberculous adhesive meningitis over left hemisphere, and a large subcortical tuberculoma associated with an abscess within the right hemisphere. Extirpation of tumor, which was nodular and adherent, and Zenker fixation of wall of abscess. Charring of surface involvement by coagulating current. Closure of wound in layers as usual.

*Pathological diagnosis.*—Metastatic carcinoma. (Figs. 3 and 4.)

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*Subsequent notes.*—Patient made a rapid recovery and was discharged free from symptoms on November 21, 1929. In January, 1930, she was admitted to the House of the Good Samaritan. At this time there was hemiplegia of the left side. There was gradual recurrence of intracranial symptoms, and death occurred March 12, 1930.

*Comment.*—The oft-recurrent tuberculosis which this girl had shown from early childhood with involvement of many sites weighed heavily in favor of a presumptive diagnosis of tuberculosis, particularly since the onset and course of her neurological symptoms so closely simulated that of the common cerebellar tuberculoma. In spite of the three-and-a-half-year interval since the breast was amputated, and the medium grade malignancy of her breast cancer, the course of such a tumor in a woman of twenty-six is ordinarily so rapidly fatal that we should doubtless have more seriously considered cancer in the differential diagnosis.

Although Van Wagenen<sup>3</sup> has shown the dangers of disseminating meningitis following operative removal of tuberculomas of the cerebellum, the electrosurgical method now at our disposal, by means of which dissection of tissue may be carried out without dissemination of inflammatory products and with simultaneous surface sterilization and sealing off of the structures traversed, offers the surgeon great opportunity in attempting a radical extirpation of such a lesion. It was for this reason that the extirpation of the supposed tubercle was undertaken in this patient rather than leaving the operation as a decompression.

*Cancer and tuberculosis.*—One cannot well report a case of coincidental carcinoma and tuberculosis without some reference to the recent revival of interest in the possibility that the two diseases are antagonistic.

The first observation of the infrequent coëxistence of cancer and tubercle is ascribed to Cruveilhier, who in 1828 concluded that the relative rarity of the double lesion was due to the widely different age-groups usually attacked by the two diseases. Rokitansky,<sup>4</sup> in 1846, as an outcome of his experience offered a theory heavily tinged with "humoral" concepts which postulated an antagonism between the tubercle "crasis" and the cancer "crasis." His astute observation that the primary site of cancer is rarely that of tuberculosis and that the converse is also true is unquestionably correct, but his assumption of the antagonism of the "crases" of the two diseases was immediately attacked, notably by Lebert<sup>5</sup> who in 1852 flatly stated that the idea was untenable because he had many times observed the coincidence of tubercle and cancer. Paget<sup>6</sup> in 1853 agreed with Rokitansky as to the antagonism of the cancerous and tuberculous "diatheses" and noted a case of a woman of twenty-five with a rapidly growing breast cancer which was surgically removed and in whom six months later both local and axillary metastases occurred with sloughing ulcerations. This situation obtained for one year and then quite suddenly healing took place, although the woman had gradually failed in strength and died two years post-operatively. At autopsy she presented extensive fulminating tuberculosis with cavitation in both apices and widespread smaller tubercles throughout the lungs in addition to fairly extensive

carcinomatous metastases in distant areas. He concluded that "the progress of the tuberculous process was commensurate with the remarkable regress of the carcinomatous extension."

The widespread influence of Rokitansky both here and abroad led to very frequent consideration of the above premise, and a precisely similar division of opinion exists today as to the frequency and infrequency of the coëxistence of the two processes, with corollary observations on the altered course of cancer when tuberculosis has been superimposed either naturally or artificially. Marked disparity in autopsy statistics on relative frequency of the diseases is explained by a failure to note the ages of the patients, the activity or extent of the tuberculosis and by failure to exhaustively search the material when once the main cause of death has been ascertained.

Bastedo<sup>7</sup> in 1904 summarized the then reported cases, and showed the following distribution of primary carcinoma associated with *active* tuberculosis mainly in lung, intestines and lymph-nodes.

|               |    |                 |    |
|---------------|----|-----------------|----|
| Breast .....  | 10 | Œsophagus ..... | 13 |
| Uterus .....  | 10 | Stomach .....   | 39 |
| Cheek .....   | 1  | Liver .....     | 8  |
| Jaw .....     | 2  | Pancreas .....  | 3  |
| Tongue .....  | 1  | Bowel .....     | 4  |
| Pharynx ..... | 1  | —               | —  |
|               |    | Total .....     | 92 |

In addition, after excluding the well-known tendency to epithelioma formation superimposed on long-standing lupus, he collected the cases in which tuberculosis and cancer existed in the same organ with the following distribution of the lesions.

|                 |    |                   |    |
|-----------------|----|-------------------|----|
| Breast .....    | 7  | Stomach .....     | 3  |
| Uterus .....    | 1  | Small bowel ..... | 3  |
| Larynx .....    | 2  | Large bowel ..... | 4  |
| Lungs .....     | 20 | Liver .....       | 2  |
| Œsophagus ..... | 4  | Rectum .....      | 3  |
|                 |    | —                 | —  |
|                 |    | Total .....       | 49 |

Moak's description<sup>8</sup> of carcinoma of the prostate in a case of pulmonary tuberculosis with subsequent distant involvement of lung, bronchial lymph-nodes, adrenal, liver and spleen by both processes, and Warthin's<sup>9</sup> report of a breast cancer with axillary metastases into a node already the seat of active tuberculosis show clearly the ability of cancer metastases to flourish in soil already involved in tubercle formation. The literature contains a great number of similar isolated reports and Broders<sup>10</sup> from his own material showed twenty cases of coëxistence of active tuberculosis and cancer, in six of which the two processes were to be observed in the same microscopic field.

The observations recorded above would appear to indicate that the two disorders coincide sufficiently often to show that there is no specific antagonism. Nevertheless, believing such an antagonism to exist, there have been

## INTRACRANIAL CARCINOMATOUS METASTASES

made isolated attempts to tuberculinize patients with carcinoma considered hopeless from any other therapeutic viewpoint. McCaskey,<sup>11</sup> in 1902, was the first to suggest this and, although citing possible improvement in one case, gave no detailed report. Dabney<sup>12</sup> in 1916 again attempted this method of therapy, and of six patients injected, noted marked improvement over a three-month interval in a young woman with an œsophageal cancer. No further clinical attempts were carried out until Delbet and Monod in 1920,<sup>13, 14</sup> in a fairly extensive and carefully conducted series of cases studied the thermal reactions in various types of cancer patients with graduated doses of tuberculin. In addition they studied the effect of tuberculin injected locally into cancer tissue, but were unable to demonstrate in either procedure any conclusive findings save the expected thermal rise. More recently statistical studies of post-mortem material have led biometricians<sup>15</sup> to feel that an antagonism was demonstrable between the two processes, and in consequence still another attempt has been made by Pearl, Sutton and Howard<sup>16</sup> to tuberculinize carcinoma patients in the hope of altering the progress of the malignancy.

### CONCLUSIONS

1. Of 1,850 verified intracranial tumors fifty-seven (3.0 per cent.) are metastatic, and of these forty-four (2.3 per cent.) are carcinomas.
2. Of forty-four metastatic intracranial carcinomas, one-fourth are primary in the breast.
3. The average age of patients with intracranial metastases from the breast is fifty-one years, the oldest being sixty-five, and the youngest thirty years old.
4. The onset of intracranial signs after primary focus in the breast averages over three and a half years, the interval ranging from three months to twelve years.
5. The course from the appearance of intracranial symptoms is rapid, fatality ensuing on an average of six months, and operative interference is survived on an average of six weeks, the longest period being five months.

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# AN ANALYSIS OF THE LYMPHADENOPATHY QUESTION WITH SPECIAL REFERENCE TO HODGKIN'S DISEASE AND TUBERCULOSIS

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RESEARCH OF NEW YORK CITY

ANY precise knowledge concerning the interrelations which many pathologists maintain exist in the group of diseases of the lymphatic apparatus must necessarily await sufficient etiological investigations to afford a sound basis for judgment. To the clinician and to the pathologist who is so associated with the clinic that he is able to follow his cases from their first appearance at the clinic to the autopsy, these diseases present widely divergent pictures, making it exceedingly difficult to classify them under a single category.

These difficulties are by no means new. Virchow,<sup>1</sup> for example, spoke of pseudoleukæmia as a "Mischmasch" and stated that the name was selected merely because one did not rightly know how the disease should be regarded and consequently threw into the pseudoleukæmia category everything of this nature which could not be interpreted otherwise. Wunderlich<sup>2</sup> was of the opinion that in the group of diseases entitled pseudoleukæmia, Hodgkin's disease, and multiple lymphadenoma without leukæmia, *manches nicht identische zusammengebracht ist*.

Our knowledge of Hodgkin's disease has been clarified, or rendered more obscure—depending on the point of view—since Sternberg<sup>3, 4</sup> demonstrated the close association of the disease with tuberculosis, and from that time on the tubercle bacillus has never been satisfactorily dissociated from the Hodgkin's picture. Von Baumgarten<sup>5</sup> undertook a classification of tuberculous lymphomata and recognized five subdivisions, namely, granular (Schuppel's), caseous, indurative, fibrocaseous, and lymphogranuloma tuberculosum. Lichtenstein<sup>6</sup> produced a lymphogranulomatous lesion associated with tuberculosis and tissue reactions of intermediate character in guinea pigs inoculated with material from the spleen of a case of pseudoleukæmic Hodgkin's with tuberculosis. In the later paper<sup>7</sup> he reviews over 200 of the older contributions on lymphogranulomatosis appearing in the literature previous to 1920.

Since that time, sporadic studies have tended more and more to favor the concept that Hodgkin's disease is a special manifestation of tuberculosis. Vasiliu and Iriminoiu<sup>8</sup> inoculated guinea pigs with material from thirteen cases. In ten of these there was no evidence of an associated tuberculosis yet the material from seven of these ten produced tuberculosis in guinea

pigs. Unfortunately the authors do not state the source of the inocula, *i.e.*, whether from nodes apt to be contaminated secondarily with the tubercle bacillus. Merle<sup>9</sup> obtained tuberculosis in a single guinea pig inoculated with material from a Hodgkin's node but again does not tell us what node. Bernard, Coste, and Lamy<sup>10</sup> produced tuberculosis in guinea pigs with emulsions of spleen and nodes from Hodgkin's disease. The source of the nodes is not given nor is it stated whether nodes and spleen were inoculated separately or together. The prevalence of tubercle bacilli in certain node groups, especially hilum and, to a lesser extent, cervical and mesenteric, is so well known that conclusions drawn from inoculations from these nodes in Hodgkin's disease must be accepted with some reservations. Coyon and Brun<sup>11</sup> report the production of Hodgkin's disease in guinea pigs by inoculation of material from the human subject. The patient likewise had tuberculosis. They are of the opinion that the diseases are unrelated. The source of their material was a mediastinal node. Martinolli<sup>12</sup> inoculated guinea pigs with material from the livers and spleens of foetuses of tuberculous mothers and obtained tuberculosis. Yet in one guinea pig he describes the finding of a typical Sternberg Hodgkin's disease and concludes that the etiological agent of the disease is a filter-passing form of the tubercle bacillus. We must admit that in our own opinion the filter-passing form of the tubercle bacillus still remains to be satisfactorily demonstrated, although the recent studies of Kahn<sup>30</sup> on the life cycle of the organism suggest further investigations of this possibility. MacMahon and Parker<sup>13</sup> have recently cultured human tubercle bacilli from a case showing the conglomerate features of leukæmia, pseudoleukæmia, lymphosarcoma, Hodgkin's disease, and tuberculosis. They wisely refrain from interpreting the picture.

Brandi<sup>14</sup> has recently described an interesting case in which tuberculosis of the testis was followed in six months by Hodgkin's disease in the inguinal nodes. L'Esperance<sup>15, 17</sup> has obtained tuberculosis in chickens, rabbits, and guinea pigs inoculated with Hodgkin's material and reports the culture of an avian tubercle bacillus from the spleen of a child with typical Pel-Ebstein disease. These results strongly suggest that the avian tubercle bacillus may be the etiological agent in certain cases, at least, of Hodgkin's disease.

During the past year one of the authors has observed a case histologically diagnosed as pseudoleukæmia. This patient was a poultryman who had repeatedly autopsied tuberculous fowls. The initial adenitis which had subsided at the time of admission, was axillary and was associated with a lesion of unknown etiology on the finger. Whereas there was no evidence of classical Sternberg Hodgkin's disease at autopsy and the histological diagnosis was pseudoleukæmia, nevertheless a node removed during the course of the disease showed a distinctly granulomatous picture with many eosinophiles but without definite Sternberg cells. This node was considered as atypical Hodgkin's disease (Case 8, Table IV). A terminal pneumococcic septicæmia was responsible for the death of all animals inoculated with the material. Such cases, in themselves not especially significant, are nevertheless of considerable

importance when viewed in the light of the gradual accumulation of rather formidable evidence tending to associate Hodgkin's disease with a tuberculous etiology.

Recent studies more directly within the field of known acid-fast etiology appear to have significance, and a possible bearing on the problem under discussion. It is now possible in experimental tuberculosis to estimate the native resistance to initial infection with a given strain of bacilli, and to predict the course of the disease in individual animals, on the basis of the monocyte-lymphocyte ratio as determined from the peripheral blood.<sup>18</sup> Animals showing a high physiological level of monocytes in contrast to lymphocytes are relatively more susceptible to acute, progressive tuberculosis than those having a low M/L index. The epithelioid cell of the tubercle has its origin from the monocyte,<sup>19</sup> and epithelioid cells as identified in the supravital technic have been found as a part of the cellular reaction in Hodgkin's nodes.<sup>20</sup>

The newer bacteriological studies of Petroff,<sup>21</sup> based upon an ingenious method for the dissociation of various pure strains of avian, bovine and human tubercle bacilli, are resulting in a reëvaluation and a new appreciation of the potentialities for variation in virulence of the acid-fast group. Standard cultures of virulent organisms, long known and studied, have been dissociated through the isolation of individual colonies. The pathology varies widely, depending upon the type of colony picked from a particular strain for inoculation purposes and the state of resistance of the animal, both of these variables now being in a fair way toward control.

Then, the correlated chemical and biological studies of the whole group of acid-fast bacilli under the direction of the Research Committee of the National Tuberculosis Association<sup>22</sup> are beginning to suggest new interpretations of the mechanism underlying the varying pathology characteristic of tuberculosis. Among the chemical partitions thus far studied, the phosphatid fraction from the lipoids, as isolated by Dr. R. J. Anderson,<sup>23</sup> of the Sterling Chemistry Laboratory, Yale University, has proven of unusual interest. Given directly into the tissues of normal animals it produces a reaction, predominantly of epithelioid cells and Langhans' giant cells, indistinguishable from that seen frequently in the disease.<sup>24</sup> However, when given intravenously in antigenic doses to rabbits the cellular response has been found to be inconstant.<sup>25</sup> As small a total dosage of the phosphatid as 5 milligrams may produce small foci of epithelioid cells in organs and tissues, while another rabbit receiving 150 milligrams in larger antigenic doses may show no cellular reaction. In the latter instance an increased ability of the blood serum to flocculate the phosphatid *in vitro* and complement-fixing antibodies<sup>26, 27</sup> have been demonstrated, together with an increased resistance to subsequent tuberculous infection.<sup>18</sup> When the antibody titre is high, with no free antigen demonstrable, tubercle formation should be minimal; but with lipoid antigen being liberated without effective neutralization or elimination by the body,

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TABLE I  
*Hodgkin's Disease Verified by Biopsy*

| Case | Age | Sex | Duration mos. | Activity  | Treated | Titre   | Remarks                                   |
|------|-----|-----|---------------|-----------|---------|---|---|
| 1    | 16  | F   | 8             | Active    | Yes     | H37A3.... 1-320<br>Av.A3.... 1-640<br>Anti H37.. 0<br>Anti Av. $\pm$ 1-20 | Fever, rapid extension, death in 4 months |
| 2    | 51  | F   | 11            | Quiescent | Yes     | H37A3.... 1-80<br>Av.A3.... 1-320<br>Anti A3... 0                         | No clinical evidence                      |
| 3    | 29  | M   | 48            | Quiescent | Yes     | Av.A3.... 1-640<br>Bov..... 1-640<br>H37A3.... 1-2560<br>Antigens... 0    | No clinical evidence                      |
| 4    | 34  | M   | 41            | Active    | Yes     | H37A3.... 1-160<br>Av.A3.... 1-80<br>Antigens... 0                        |   |
| 5    | 48  | M   | 7             | Active    | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640  |   |
| 6    | 48  | M   | 36            | Quiescent | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640  | Active pulmonary tuberculosis             |
| 7    | 22  | M   | 5             | Active    | Yes     | H37A3.... 1-320<br>Av.A3.... 1-1280                                       |   |
| 8    | 24  | F   | 36            | Quiescent | Yes     | H37A3.... 1-1280<br>Av.A3.... 1-1280<br>Anti H37.. 0<br>Anti Av... 1-10   | Now rapidly progressive                   |
| 9    | 45  | M   | 6             | Active    | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640<br>(avian heavier)                     |   |
| 10   | 28  | F   | 50            | Active    | Yes     | H37A3.... 1-640<br>Av.A3... $\pm$ 1-640                                   | Hæmoptysis; pyelitis; bone involvement    |
| 11   | 29  | F   | 40            | Active    | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640<br>Anti H37.. 1-40<br>Anti Av... 1-40  |   |
| 12   | 19  | M   | 27            | Active    | Yes     | H37A3.... 1-640<br>Av.A3.... 1-320<br>(avian heavier)                     | Probably thymic with malignant features   |
| 13   | 21  | F   | 29            | Active    | Yes     | H37A3.... 1-2000<br>Av.A3.... 1-1000                                      | Progressive; death 8 months later         |
| 14   | 21  | F   | 4             | Active    | Yes     | H37A3.... 1-40<br>Av.A3.... $\pm$ 640<br>Av.A3.... 1-320<br>$\pm$ 1280    | Febrile; death in 11 months from onset    |

## HODGKIN'S DISEASE AND TUBERCULOSIS

TABLE I (Continued)

| Case | Age | Sex | Duration mos. | Activity   | Treated | Titre  | Remarks                               |
|------|-----|-----|---------------|------------|---------|--|---------------------------------------|
| 15   | 27  | M   | 13            | Active     | Yes     | H37A3.... 1-250<br>±640<br>Av.A3.... 1-320                               | Early recurrent phase after treatment |
| 16   | 40  | M   | 18            | Quiescent  | Yes     | H37A3.. ±1-40<br>Av.A3... ±1-40  | Anti Av. suggestive; others—o         |
|      |     |     |               | Active     | Yes     | H37A3.... 1-160<br>Av.A3.... 1-640<br>Bov..... 1-40                      |                                       |
| 17   | 16  | M   | 72            | Active     | Yes     | H37A3.... 1-160<br>Av.A3.... 1-1280<br>Anti H37.. ±<br>Anti Av... +++    |                                       |
| 18   | 28  | F   | 36            | Active     | Yes     | H37A3.... 1-160<br>Av.A3.... 1-640<br>Antigens... o                      |                                       |
| 19   | 40  | M   | 36            | Active     | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640<br>Antigens... o                      | Bone lesions                          |
| 20   | 31  | M   | 4             | Regressing | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640<br>Anti H37.. o<br>Anti Av... +       |                                       |
| 21   | 45  | F   | 18            | Active     | Yes     | H37A3.... 1-320<br>Av.A3.... 1-320<br>Anti H37.. o<br>Anti Av... +       |                                       |
| 22   | 57  | M   | 3             | Active     | Yes     | H37A3.... 1-160<br>Av.A3.... 1-320<br>Antigens... o                      |                                       |
| 23   | 22  | F   | 8             | Active     | Yes     | H37A3.... 1-1280<br>Av.A3.... 1-1280<br>Bov..... 1-1280<br>Antigens... o |                                       |
| 24   | 23  | M   | 5             | Regressing | Yes     | H37A3.... 1-1280<br>Av.A3.... 1-640<br>Bov..... 1-160<br>Antigens... o   |                                       |

new foci of epithelioid cells arise, within which the tubercle bacilli appear to survive and multiply with little difficulty.

Comparable phosphatid fractions from human,<sup>27</sup> bovine<sup>28</sup> and avian tubercle<sup>29</sup> bacilli have been isolated by Doctor Anderson and his associates, parallel biological studies having been made by Doctor Sabin and associates at the Rockefeller Institute. It has been determined that this particular lipid fraction, as obtained from all three sources, contains the potentialities for inducing tissue proliferation, primarily epithelioid in character, and may possess anti-

genic properties. Which of these two reactions, the serological or the foreign body tissue response, will predominate, is dependent upon the constitution of the individual animal.

In testing sera from tuberculous sources of known human or bovine etiology the titre has been higher usually with the homologous antigen, though phosphatid of eterologous origin has been precipitated in relatively high dilution also. Absorption experiments have indicated incomplete precipitation with heterologous, as contrasted with homologous antigens.<sup>26</sup> Further chemical and biological studies are in progress to establish whether the phosphatid fractions from human bovine and avian tubercle bacilli are qualitatively, or only quantitatively, different.

In a study during the past two years of more than 350 clinical cases, of which the majority were tuberculous, frequent ability to precipitate the tuber-

TABLE II  
*Clinical Hodgkin's Disease (No Biopsies)*

| Case | Age | Sex | Duration | Activity          | Treated | Titre  | Remarks                                     |
|------|-----|-----|----------|-------------------|---------|--|---|
| 1    | 16  | M   | 17 mo.   | Quiescent         | Yes     | H37A3.... 1-40<br>±1-160<br>Av.A3.... 1-160<br>Anti H37.. 1-640*                                   | Later suspect this hilum tbc.               |
| 2    | 28  | F   | 36 mo.   | Active            | Yes     | H37A3.... 1-640<br>±1-1280<br>Av.A3.... 1-2000   | Terminal phase                              |
| 3    | 38  | F   | 4 mo.    | Early, regressing | Yes     | H37A3.... 1-320<br>±1-640<br>Av.A3.... ±1-2000<br>(2 hrs)<br>1-320<br>(24 hrs)<br>Bov.A3.... 1-320 |   |
| 4    | 42  | M   | 23 mo.   | Active            | Yes     | H37A3.... 1-1280<br>(2 hrs)<br>Av.A3.... 1-640<br>H37A3.... 1-320<br>(24 hrs)                      | Classical course.<br>Dead                   |
| 5    | 36  | F   | 5 yrs.   | Active            | Yes     | H37A3.... 1-160<br>Av.A3.... 1-160   | Classical course.<br>Dead                   |
| 6    | 28  | M   | 48 mo.   | Regressing        | Yes     | H37A3.... 1-320<br>Av.A3.... 1-640<br>Bov..... 1-160   | Classical course.<br>Now fever and pruritis |
| 7    | 22  | F   | 40 mo.   | Quiescent         | Yes     | H37A3.... 1-640<br>Av.A3.... 1-640<br>Anti H37.. 0<br>Anti Av... 1-10                              |   |
| 8    | 16  | M   | ?        | Active            | Yes     | H37A3.... 1-2560<br>Av.A3.... 1-2560<br>Anti H37.. ±<br>Anti Av... ++                              |   |

\* In this instance a 1-640 dilution of patient's serum against undiluted immune rabbit serum.

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culo-phosphatid in high titre, or the precipitation with a phosphatid antiserum of suspected uncombined antigen, has been demonstrated. Spinal fluids pleural effusions, joint fluids, as well as blood sera have been tested. In a study of tuberculous children and of children vaccinated with Calmette-Guérin bacillus<sup>31</sup> a reciprocal relationship between the monocyte-lymphocyte ratio and the phosphatid antibody titre in the blood serum has been noted. In tuberculous children when the antibody titre has been low and the M/L index high the patients have been clinically ill, whereas improvement has followed a rise in the antibody titre and an accompanying fall in the M/L ratio.

As a part of the clinical study for an evaluation of this phosphatid precipitin test in diagnosing and following tuberculous infection, we have recorded the reaction of the blood sera from a group of patients at the Memorial Hospital, New York City, showing lymphadenopathies of diverse pathological diagnosis. The cases were seen, the blood serum collected and the precipitin tests read, in the majority of instances, before the results of the biopsy findings and the clinical diagnoses were known. The analysis of the accumulated observations is presented in Tables I to VII inclusive.

Fifty-five cases comprise this series, of which twenty-four fall into the group of Hodgkin's disease as verified by biopsy examination (Table I), and eight additional cases have had a similar clinical diagnosis without histopathological confirmation (Table II). The remaining twenty-three cases

TABLE III  
*Lymphosarcoma*

| Case | Age | Sex | Duration | Treated | Active | Titre   | Remarks                                       |
|------|-----|-----|----------|---------|--------|---|---|
| 1    | 51  | M   | 5 yrs.   | Yes     | No     | H37A3..... 1-80                                     | Verified                                      |
| 2    | 35  | M   | 5 mos.   | Yes     | No     | H37A3..... 1-40<br>Av.A3..... 1-40<br>Antigens... 0 | No biopsy                                     |
| 3    | 50  | F   | 12 mos.  | Yes     | Yes    | H37A3..... 1-40<br>±1-80                            | Verified                                      |
| 4    | 34  | F   | 5 mos.   | Yes     | No     | H37A3..... 1-40                                     | Mediastinal. No biopsy                        |
| 5    | 24  | M   | 12 mos.  | Yes     | No     | H37A3..... 1-320                                    | Tonsillar, primary                            |
| 6    | 64  | M   | 2 mos.   | Yes     | Yes    | H37A3..... 1-80<br>Av.A3..... 1-80<br>Antigens... 0 | Verified. Death in 4 months                   |
| 7    | 63  | M   | 6 mos.   | Yes     | No     | H37A3..... 1-640<br>Av.A3..... 1-160                | Verified. No clinical sign of tbc. X-ray neg. |
| 8    | 51  | M   | 6 wks.   | Yes     | Yes    | H37A3..... 1-40<br>±160<br>Av.A3..... 1-160         | Verified                                      |
| 9    | 48  | M   | 4 mos.   | Yes     | Yes    | H37A3..... 0<br>Av.A3..... 0                        | Verified                                      |
| 10   | 52  | F   | 7 mos.   | Yes     | Yes    | H37A3..... 0<br>Av.A3..... 0                        | Verified                                      |



include a variety of pathological conditions involving the lymphatic system, and have been classified partially on biopsy findings, partially on clinical signs and symptoms (Tables III to V; see footnote Table IV).

The difficulty with which activity of the pathological process is measured in a chronic condition such as Hodgkin's disease, together with the influence of intensive irradiation therapy, makes any correlation between the precipitin titre and resistance impossible in this series. Repeated observations on the same case, such as in No. 16, Table I are necessary before any conclusions

TABLE IV  
*Lymphatic Leukæmia, Pseudoleukæmia, and Leukosarcomatosis (Sternberg)*

| Case | Type*              | Age | Sex | Duration     | Activity† | Titre  | Remarks                         |
|------|--------------------|-----|-----|--------------|-----------|--|---------------------------------|
| 1    | Lymphatic leukæmia | 55  | M   | 3 mos.       | Active    | H37A3.... 1-80   |                                 |
| 2    | Lymphatic leukæmia | 27  | M   | 4 mos.       | Active    | H37A3.... 1-320<br>Av.A3.... 1-80<br>Antigens... 0                   |                                 |
| 3    | Lymphatic leukæmia | 53  | M   | 14 mos.<br>? | Active    | H37A3.... 1-80   |                                 |
| 4    | Leukosarcomatosis  | 42  | M   | 9 mos.       | Active    | H37A3.... 1-80<br>Av.A3.... 1-80<br>Antigens... 0                    |                                 |
| 5    | Leukosarcomatosis  | 53  | M   | 10 mos.      | Active    | H37A3.... 1-160<br>Av.A3.... 1-160                                   |                                 |
| 6    | Pseudo-leukæmia    | 54  | M   | ?            | Active    | H37A3.... 1-1280<br>Av.A3.... 1-80                                   |                                 |
| 7    | Pseudo-leukæmia    | 50  | F   | 47 mos.      | Active    | H37A3.... 1-160<br>Av.A3.... 1-40<br>Antigens... 0                   |                                 |
| 8    | Pseudo-leukæmia    | 36  | M   | 13 mos.      | Active    | H37A3.... 1-320<br>Av.A3.... 1-640<br>(2 hrs.)<br>1-160<br>(24 hrs.) | Node classed atypical Hodgkin's |

\* To pathologists who realize the changing pictures one encounters in the course of these loosely classified disease conditions it will be quite apparent that it is impossible to group them properly. They change as the disease progresses. As given in the tables the grouping applies to the temporary clinical classification at the time the tests were done.

† Often activity is not determinable. Hodgkin's disease, quiescent so far as external manifestations go, may be active in deep, non-palpable abdominal nodes, bone marrow, etc. No one knows enough about pseudo-leukæmia to say when it is or is not active. We have presumed activity if the blood count varied from the normal. Similar difficulties are presented throughout the whole group of diseases.

are justified. However, the general tendency toward a high antibody titre in this group is consonant with a chronic disease process if interpreted in terms of similar findings in tuberculosis. In nine instances the presence of free phosphatid antigen was suggested in tests with antisera for avian phosphatid, four of the cases giving also a positive precipitin reaction with anti-human tuberculo-phosphatid serum. This observation would lend support to L'Esperance's finding of the avian tubercle bacillus in certain Hodgkin's cases. It is a possibility, of course, that non-tuberculous processes could so alter

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the blood serum that the physico-chemical precipitation of the colloidal suspension of tuberculo-phosphatid would occur. However, it seems less likely that an apparently specific antiserum secured from rabbits, which had been treated with intravenous antigenic doses of this phosphatid, should react with a patient's serum, if a similar antigen was not present. The serum from normal rabbits has not reacted with normal or tuberculous human serum in our experience.

In Table VI are summarized the antibody titres to tuberculo-phosphatid as given under each diagnostic division, and it is here that certain striking differences are to be noted. Twenty-six of the thirty-two cases of Hodgkin's

TABLE V  
*Heterogeneous Lymphadenopathies*

| Case | Type                   | Age | Sex | Duration                | Activity   | Titre   | Remarks  |
|------|------------------------|-----|-----|-------------------------|------------|---|--|
| 1    | Lymphoma               | 57  | F   | 12 mos.                 | Quiescent  | H37A3... 1-40<br>Av.A3.... 1-40<br>Antigens.. 0 | Undetermined etiology  |
| 2    | Chronic lymphadenitis  | 56  | F   | 24 mos.                 | Regressing | H37A3... 1-160<br>Av.A3.... 1-160               |  |
| 3    | Undiagnosed adenopathy | 18  | F   | 24 mos. on entry (1925) | Quiescent  | H37A3... 1-320<br>Av.A3.... 1-640               | Radiosensitive. May have been Hodgkin's. No evidence in June, 1930 |
| 4    | Tuberculous adenitis   | 28  | M   | 5 mos.                  | Active     | H37A3... 1-640<br>Av.A3.... 1-320               |  |
| 5    | Tuberculous adenitis   | 28  | F   | 24 mos.                 | Quiescent  | H37A3... 1-40<br>Av.A3.... 1-40                 | No evidence of clinical disease when tested                        |

*Explanation for abbreviations, Tables I-V.*

H37—the H37 strain of human tubercle bacilli.

Av.—avian tubercle bacilli.

Bov.—bovine tubercle bacilli.

A3—Anderson's phosphatid fraction, original concentration 1 per cent. suspension.

Anti H37, anti A3, etc.—reaction between patient's serum and immune rabbit serum prepared by immunizing rabbits against the A3 phosphatid.

disease showed a capacity of the blood serum to precipitate the phosphatid in a dilution of 1-640 (of an original 1 per cent. suspension), or higher. This is well within the range of positive reactions observed in known tuberculous cases. Only three of the twenty-three cases, which were not of the Hodgkin's type, showed a similar precipitating ability, and one of these was an active case of tuberculous adenitis (Case 4, Table V), and another an undiagnosed adenopathy suggestive of Hodgkin's disease (Case 3, Table V). Two of the cases in the miscellaneous group, which were diagnosed clinically, when first seen, as Hodgkin's disease, were reported with low, 1-40, 1-80, precipitin titres previous to the biopsy diagnosis of lymphosarcoma. The coincidence, if such it be, between a high anti-phosphatid titre in the serum and

the presence of Hodgkin's disease has been sufficiently frequent in this series to raise the question of the correctness of this diagnosis in the adenopathy group, when the precipitin reaction has been negative, or positive only in the non-specific range. With reference to an etiological relationship between the tubercle bacillus and Hodgkin's disease we are not unmindful of the frequency with which true tuberculous disease has been found associated with the typical pathological picture of Hodgkin's and the suggestive results of these tests may hardly more than emphasize this long-recognized relationship.

TABLE VI  
*Analysis of Results with Tuberculo-phosphatid*

| Type of disease                   | Titres       |              |              |               |               |
|-----------------------------------|--------------|--------------|--------------|---------------|---------------|
|                                   | 160 or above | 320 or above | 640 or above | 1280 or above | 2000 or above |
| Verified Hodgkin's.....           | 24 of 24     | 23 of 24     | 20 of 24     | 8 of 24       | 2 of 24       |
| Clinical Hodgkin's—no biopsy..... | 8 of 8       | 6 of 8       | 6 of 8       | 4 of 8        | 3 of 8        |
| Lymphosarcoma.....                | 2 of 8       | 2 of 8       | 1 of 8       | 0             | 0             |
| Pseudoleukæmia.....               | 3 of 3       | 2 of 3       | 2 of 3       | 1 of 3        | 0             |
| Lymphatic leukæmia....            | 0            | 1 of 3       | 0            | 0             | 0             |
| Leukosarcomatosis.....            | 1 of 2       | 0            | 0            | 0             | 0             |

It will be seen from Table VII that in less than half of the cases of Hodgkin's disease was the titre for avian phosphatid higher than that for the human lipid, though in nineteen of the twenty-four verified cases the avian titre was equal to, if not above, that of the human. Biologically the phosphatids from both sources produce an identical reaction of epithelioid cells in the connective tissues of normal rabbits, and no qualitative differences have as yet become apparent in the experimental studies.

TABLE VII  
*Specificity of Antigens*

| Type of disease           | Avian titre higher | Avian equals human | Human titre higher |
|---------------------------|--------------------|--------------------|--------------------|
| Verified Hodgkin's.....   | 10 of 24           | 9 of 24            | 5 of 24            |
| Hodgkin's unverified..... | 4 of 8             | 3 of 8             | 1 of 8             |
| Pseudoleukæmia.....       | 1 of 3             |                    | 2 of 3             |

Hodgkin's disease is comprised of several heterogeneous but interlocking pathological manifestations. It may be an ill-defined chronic lymphadenitis with slight to moderate reticulum cell overgrowth, or proliferation of the sinus endothelium, and a slight eosinophilic infiltration, or it may present as a more or less diffuse overgrowth of small lymphocytes associated with a low-grade pseudoleukæmic blood picture; but, in the fully developed, typical types, there is the characteristic Sternberg cell histology, and on occasion a tendency toward various sarcomatoid manifestations. When studied supravitaly,<sup>20</sup> nodes from cases seen early in the disease show many epithelioid cells entirely

## HODGKIN'S DISEASE AND TUBERCULOSIS

characteristic of those found in tuberculosis. In the later stages of the disease there are perhaps fewer epithelioid cells and a more general connective tissue reaction. Differences between these pictures and classical caseous tuberculosis are striking only when the extremes are considered. There are many examples which reveal interrelationships, and cases in which it is quite impossible to determine where one type ends and the other begins. Hodgkin's disease differs from typical tuberculosis hardly more than the various manifestations of clearly recognized tuberculosis differ from one another—no more than pleurisy with effusion differs from phlyctenule, or hyperplastic tuberculosis of the cæcum from acute pneumonic phthisis or lupus erythematosus.

That Hodgkin's disease pursues an inevitably fatal course is scarcely a sound argument against a tuberculous etiology. In the first place, it is never treated as is tuberculosis; secondly, involvement is usually extensive when patients are first seen; and in the third place, it is impossible to estimate the number of transient lymphadenopathies never subjected to microscopic diagnosis, which if so studied, might show features which would necessitate the diagnosis of Hodgkin's disease. We, personally, have known one patient (biopsy verification), who survived gland excision seventeen years, and who now has a local recurrence of the process with some dissemination, but who gives promise of surviving many years longer.

With the newer histo-pathological approach to the finer cellular differentiation and structure in disease processes, which is now possible through the use of supravital staining with its additional criteria, we may hope eventually to understand more fully the meaning of these reactions of diverse etiology in terms of physiological equilibria and resistance. The body has at its disposal only a limited number of cells with which to combat invasion and insult from whatever source, and this is the underlying reason for the confusion which attends the attempt at differentiation in such a closely allied group of diseases as those affecting the lymphatic system.

The recent work of Petroff<sup>32</sup> on the bacteriology of the acid-fast bacilli necessitates a restudy of this group of organisms in their relationship to human disease. A careful comparative study of the protein antigens (allergy and skin hypersensitiveness) from the several "R" and "S" strains of tubercle bacilli is now essential, and quite possible. The differing pathology, which has already been found to accompany the various combinations of constitutional resistance and these diverse types of infecting organisms, presents a fertile field for present speculation and future investigation.

An ultimate understanding of both the pathological agent or factor, and the mechanism of adjustment or resistance must precede any final approach toward the control of each definite etiological entity in disease.

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# THE GENETIC NEOPLASTIC RELATIONSHIPS OF HODGKIN'S DISEASE, ALEUKÆMIC AND LEUKÆMIC LYMPHO-BLASTOMA, AND MYCOSIS FUNGOIDES

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IN 100,000 diagnostic tissue examinations made in the Pathological Laboratory of the University of Michigan between the years 1895 and 1927 there were 506 cases, approximately 0.5+ per cent. of all cases, diagnosed as Hodgkin's disease, aleukæmic and leukæmic lymphoblastoma, and mycosis fungoides. These cases were further distributed, as to diagnosis, as follows:

## *Hodgkin's*

|  |     |
|--|-----|
| Typical Hodgkin's  | 94  |
| Atypical Hodgkin's   | 83  |
| Sarcomatous Hodgkin's  | 29  |
| Leukæmic Hodgkin's, lymphatic                                    | 6   |
| Leukæmic Hodgkin's, myelæmic                                     | 2   |
| Hodgkin's becoming lymphosarcoma                                 | 12  |
| Abdominal Hodgkin's  | 3   |
| Hepatic Hodgkin's, cirrhosis                                     | 2   |
| Cutaneous Hodgkin's, mycosis                                     | 1   |
| (Non-caseating tuberculosis with clinical diagnosis of Hodgkin's | 10) |

## *Lymphoblastoma (lymphosarcoma)*

|   |     |
|---|-----|
| Typical glandular lymphoblastoma                          | 134 |
| Typical abdominal lymphoblastoma, gastro-intestinal, etc. | 26  |
| Typical tonsillar lymphoblastoma                          | 19  |
| Typical aleukæmic lymphoblastoma becoming leukæmic        | 9   |
| Atypical glandular lymphoblastoma                         | 44  |

## *Mycosis fungoides*

|  |    |
|--|----|
| Aleukæmic lymphoblastoma                   | 23 |
| Aleukæmic lymphoblastoma becoming leukæmic | 5  |
| Aleukæmic myeloblastoma                    | 1  |
| Leukæmia cutis                             | 3  |

During the same period, in 2,000 autopsies there were 83 (4.1 per cent.) cases falling into the same diagnostic categories, as follows:)

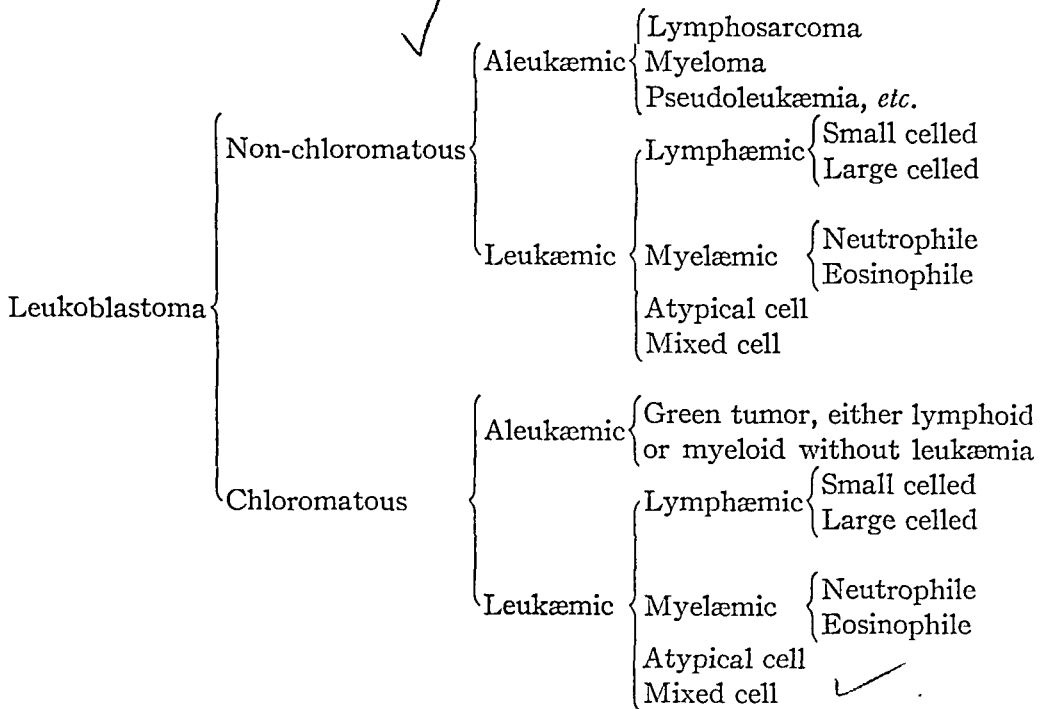
|   |      |
|---|------|
| Myelæmic leukæmia                         | 24   |
| Leukæmic lymphoblastoma                   | 20 ✓ |
| Aleukæmic lymphoblastoma                  | 20 ✓ |
| Hodgkin's, typical                        | 7 ✓  |
| Aleukæmic mycosis fungoides               | 5    |
| Leukæmic mycosis fungoides                | 3    |
| Hodgkin's mycosis fungoides               | 1    |
| Plasma-celled mycosis fungoides           | 1    |
| Myeloid mycosis fungoides                 | 1    |
| Eosinophile (myeloctye) mycosis fungoides | 1    |

(The study of this material, as outlined above, has formed the basis for the writer's belief that Hodgkin's disease is a neoplasm and related genetically to the lymphoblastomas, of which both the aleukæmic and the leukæmic forms are identical pathologically; and that mycosis fungoides is likewise a neoplasm belonging to the same generic group. The essential differences between these different clinical forms consist in different degrees of differentiation or entdifferntiation, and the organ or tissue primarily involved. Transition forms exist between all of these groups, and one type may be transformed into another.) Clinically they all possess the characters of malignancy; no cure is known for any one of them; they progress inevitably to a fatal termination, sometimes rapidly, sometimes very slowly. They all show infiltrative tendencies and metastasize, ultimately involving all of the reticulo-endothelial and blood-cell forming tissues of the body. They show an abundance of mitotic cell-division figures, both typical and atypical, as well as amitotic cell division. Their growth is at times rapid, at other times slow; they are characterized by their marked tendency to degenerations and necrosis. Marked fibrosis often follows the degenerative changes. At times the regressive tendencies are so marked that so great a reduction in size of the growths takes place, that clinically they may become so greatly diminished in size as apparently to disappear. A certain degree of fever frequently accompanies such periods of marked retrogression. Periods of the aleukæmic state may alternate with leukæmic periods. The acute transformation into a leukæmia is sometimes preagonal. The general effects upon the patient are in every way comparable to those of tumor cachexia; progressive anæmia, emaciation, weakness and exhaustion. (Although regarded many times as representing infectious processes, no organism described as a possible etiologic factor has ever met the test; moreover, the clinical and pathologic pictures presented are those of a progressive fatal malignancy.) No mild cases exist; no cures have ever been observed for any one of the forms belonging to this group. There is no evidence of any immunity process; no specific antibodies are found in the serum. (In all of these forms the pathologic picture is that of a progressive increase of atypical tissue replacing the normal tissues of the body, up to a point at which life is no longer possible, or secondary complications may end the picture.)

(More than twenty-five years ago the writer's study of chloroma convinced him that "Chloroma is a tumor-like hyperplasia of the parent-cells of the leucocytes, primary in the red marrow, the periosteum being involved only secondarily." This was new pathology at the time, but this view has been generally accepted since. (In 1904 he observed an aleukæmic lymphosarcoma (lymphoblastoma), primary in the intestine, become transformed into the leukæmic stage after a surgical operation for removal of the appendix.) This case was reported in the *Transactions* of the Association of American Physicians, in 1904, under the title of "The Neoplasm Theory of Leukemia, with Report of a Case Supporting This View." It was regarded by the writer as presenting the same evidence of malignant neoplasm nature, in its infiltrations and metastases, as did the chloroma case, and in this article he

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made the statement that "leukemia must be regarded as a neoplastic hyperplasia of the parent cells of the blood cells." For this neoplasm, he suggested the term *leukoblastoma*, and offered the following classification of the leukæmic and aleukæmic neoplasms:



This was at a time when no textbook considered the possibility of the neoplastic nature of leukæmia, but a certainty of conviction as to the correctness of this view has remained in the writer's mind ever since, and he has had in recent years the satisfaction of seeing an increasing acceptance of this view. In spite of the prevailing universal belief that Hodgkin's disease was an infective granuloma, he very early was led to include this disease in the same group with the aleukæmic and leukæmic lymphosarcomas, because of observed cases showing such transitions from typical Hodgkin's into the other forms.) His experience was the same as far as mycosis fungoides was concerned, and this clinical form he brought also into the same group of generic relationship. While the limits of this paper are too brief to enter into any detailed description of epoch-making cases observed, or into extended arguments over the relationship of the different forms, an attempt will be made to give a concise and succinct statement of the writer's views on this question, and the chief reasons in support of these views.

*Hodgkin's Disease.*—Typical Hodgkin's presents a characteristic and easily recognizable histological picture. The most marked feature is at first a localized or focal proliferation of the reticulum with the presence of atypical lymphocytes, lymphoblasts, plasma cells, mononuclear and polynuclear eosinophiles, myeloid cells, fibroblastic cells, and the multinucleated "Hodgkin's" or "Dorothy Reed" giant cell, which resembles those of the bone-marrow. These and the eosinophile cells constitute the chief diagnostic factors microscopically; and our diagnoses of typical Hodgkin's rests upon their presence and is never made in their absence. As the disease becomes more chronic these foci in these lymph-nodes become more fibrous, the struc-



ture of the node is wholly lost, and its appearance becomes that of a multi-centric nodular mass, the active nodules separated from each other by dense fibrous connective tissue. In the more actively growing cellular forms degeneration and necrosis occur frequently; often these degenerative changes are so marked that a great reduction in their size, even to that of the normal node, may result. The disease may begin anywhere in the body where there is primitive lymphoid tissue or reticulo-endothelial tissue. In our experience the left cervical nodes have been most often the clinical point of origin; then the right cervical region; then the axillary, inguinal, mediastinal, and retroperitoneal nodes in the order named. The process may also be primary, or at least most marked, in the tonsil, thymus, bone-marrow, spleen, liver and skin. We have diagnosed Hodgkin's in the tonsil before any enlargement of the lymph-nodes was clinically apparent. Ultimately, all of the lymphoid tissue in the body is involved in the process, and throughout the reticulo-endothelial tissues of the peri-lymph-node adipose tissue, in the mediastinum, retroperitoneal adipose tissue, and subcutaneous fat, small nodules, or more diffuse infiltrations, showing the same histologic structure as the lymph-nodes develop. Even in the meninges Hodgkin's foci may be present. In old and advanced cases the liver may present the appearance of a Hodgkin's cirrhosis; even in the kidneys and testes metastatic nodules and infiltrations may be found. The lungs may also not infrequently show numerous typical Hodgkin's nodules and infiltrations. The heart usually escapes, but even in this organ we have found small Hodgkin's nodules, and in one case of mediastinal Hodgkin's (thymoma) the heart showed marked involvement. Further, in late Hodgkin's atypical cells are found in small masses in the splenic, kidney and liver capillaries, apparently free, or forming small emboli, proving beyond any doubt the occurrence of metastasis. When recognized clinically the disease is as a rule well advanced and the majority of the lymph-nodes show the typical lesion. As the lymph-nodes become progressively replaced by the atypical tissues, all normal lymph-node structure disappears, the sinuses are obliterated, the germ centres are lost, and the distinction between cortex and medulla can no longer be made out. Around the nodes so altered there is a progressive new formation of lymphoid tissue which in turn becomes involved in the process. After removal of diseased nodes there occurs a similar regeneration of nodes that ultimately show the characteristic changes of the disease. Not all cases of Hodgkin's show a febrile reaction, but in the majority there is an irregular fever curve, especially marked in the case of degenerating nodes. Secondary infection of the necrotic areas is undoubtedly responsible for the septic fever curves and night sweats found in some cases. The disease occurs most frequently in the young adult; our earliest case was in a child three years old, and the oldest in a male of seventy. It is relatively uncommon after the age of forty. The usual limit of life after relatively early diagnosis is three to five years. X-ray irradiation is the only treatment that will prolong life; in some cases under constant and experienced supervision the limit of life has been extended to seven, nine, ten and twelve years. In spite of repeated irradiation the disease process ultimately conquers, and in

these late cases there is an extraordinary extension of the lesions to practically all organs and tissues. In two of our X-ray cases there occurred a transformation of the pathological lesions into those of myelæmic leukæmia; in six other cases lymphatic leukæmia developed spontaneously without X-ray irradiation. There were three primary abdominal Hodgkin's in this series, involving particularly the spleen, a splenomegaly being the chief clinical feature; and the disease was diagnosed in this organ after splenectomy, which was followed by a gradual generalization of the process. In two cases the chief clinical symptoms were hepatic, and microscopic examination of the enormously enlarged livers showed typical Hodgkin's involvement of all the periportal tissues—a pathological picture justifying the use of the descriptive term, Hodgkin's cirrhosis. The spleen showed similar lesions in these cases, and Hodgkin's foci were found in the lymph-nodes and bone-marrow, but nowhere to the extent shown in the liver. Further, in one clinical case of mycosis fungoides the skin lesions were typically those of Hodgkin's. In ten cases diagnosed clinically as Hodgkin's, a diffuse miliary non-caseating tuberculosis was found in the excised nodes. One of these cases treated twenty-five years ago with old tuberculin recovered and is still alive.

As atypical Hodgkin's we designate cases in which the atypical myeloid cells, "Dorothy Reed" cells and eosinophiles are either few in number or absent. The focal or nodular replacement of the lymph-nodes by fibrous connective tissue, or atypical lymphoid tissue, with all of the clinical picture of Hodgkin's, constituted the basis for the diagnosis of Hodgkin's and clinical observation confirmed this in the majority of these cases. Of a few cases in which biopsies were secured months or years later, some showed typical Hodgkin's lesions, others the microscopic picture of lymphosarcoma or reticulocytosarcoma; for the græter part this group represents transition forms to the sarcomatous type of lesion, and we would today place them in this category.

By sarcomatous Hodgkin's we mean very actively growing, diffusely cellular rather than nodular lesions, with few or no eosinophiles or Dorothy Reed cells, and a greater tendency to infiltrate and to metastasize, particularly in the kidneys and lungs. The sarcomatous transformation of a Hodgkin's may proceed in one of two directions, either leading to a lymphosarcoma or to a large-celled form, with abundant reticulum and numerous giant cells, which we have styled a reticulocytoma or reticulo-endothelioblastoma. The former arises through the overproduction of maternal lymphoblasts, the resulting growths being typical lymphoblastomas (lymphosarcomas), either small celled or large celled. All lymph-node structure is lost, the germ centres and sinuses disappear, cortex and medulla become converted into a uniform mass of atypical lymphocytes with many large maternal lymphoblasts scattered throughout, and there is an infiltration of the capsule and pericapsular tissues. Ultimately, in place of the Hodgkin's lesion all of the lymphoid tissues of the body assume the character of the lymphoblastoma. In twelve of our cases repeated biopsies showed the progress of this transformation from a typical Hodgkin's to a typical lymphoblastoma, with com-

plete absence of eosinophiles, giant cells, myeloid cells, and disappearance of the reticulum. Usually the resulting lymphoblastoma is aleukæmic, but in six of our cases there gradually developed the blood picture of a lymphatic leukæmia. In the reticulo-endothelioblastoma form, the lymphoid cells become reduced in number, the eosinophiles disappear, and the majority of the cells come to be large polymorphic cells with abundant cytoplasm, and possessing many large hyperchromatic nuclei. Numerous giant cells of the myeloid type occur, and the appearances may be those of a large round-cell sarcoma of malignant type. The reticulum is usually very abundant and prominent, forming an interlacing network of coarse fibrils in the spaces of which lie the sarcoma cells. This form shows a greater degree of malignancy than either the type Hodgkin's or the lymphoblastoma. It is especially likely to develop metastases in the kidneys, and the spleen is involved earlier than in the other two forms. In some cases a rapid enlargement of the liver results

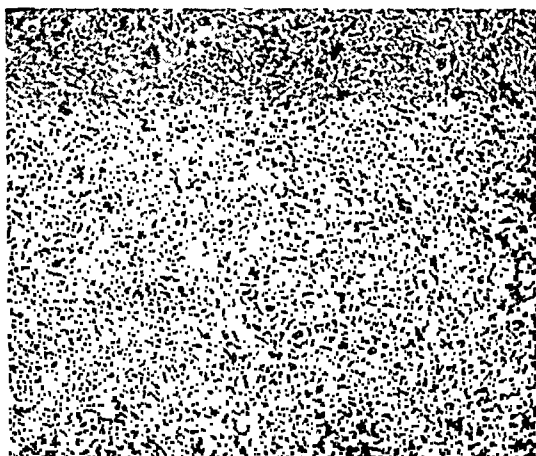


FIG. 1.—Transformation of a Hodgkin's into a reticulocysto-endothelioblastoma. Ultimately all traces of the Hodgkin's lesion disappeared.

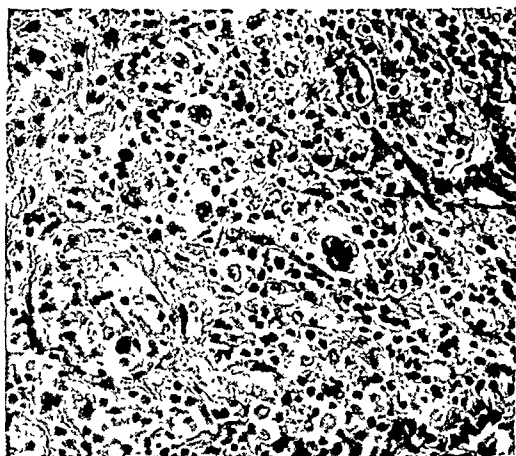


FIG. 2.—Sarcomatous Hodgkin's. Transformation into reticulocysto-endothelioblastoma.

from the marked infiltrations of the periportal tissues. In our material there were twenty-nine cases of this type of sarcomatous Hodgkin's, and in a number of these the process has been followed in successive biopsies extending over a number of years, in one case over seven years (controlled by X-ray irradiation). We have seen one case of this type proceed to a rapidly fatal termination in a child just over one year of age, the lesions presenting from the beginning the histologic picture of the reticulo-endothelioblastoma. Without irradiation the clinical course of this type is usually more malignant and shorter. Finally, in irradiated cases of Hodgkin's, after some years, the Hodgkin's lesion may be replaced by the sarcomatous, and the case be brought to a speedy termination. In the one case of Hodgkin's mycosis fungoides seen by us, typical Hodgkin's lesions were found in the cutaneous growth and in the lymph-nodes. The clinical history of this case was characteristic of mycosis fungoides, with a ten-year pre-mycotic stage of skin lesions before the development of the fungating growths.

*Lymphoblastoma (Lymphosarcoma).*—In one hundred and thirty-four cases of biopsies from enlarged lymph-glands microscopic examination showed

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the presence of typical lymphoblastoma. (In the majority of these the left cervical region was primarily involved, or showed a more advanced stage of the disease. In twenty-six cases the growths were apparently primary in the gastro-intestinal tract. Nineteen cases were diagnosed in the routine examination of tonsils, and later showed enlargement of the cervical nodes. One of these cases lived for seventeen years after the diagnosis had been made upon his enlarged tonsil, dying ultimately of generalized lymphoblastoma. Another case lived for thirteen years after the tonsil diagnosis, dying with generalized lymph-node enlargement. In both of these cases the extension of life was undoubtedly due to the systematic use of X-ray irradiation. Microscopically, all of these cases presented the same histologic picture, an atypical diffuse lymphoid hyperplasia (usually small celled) with loss of germ centres and normal architecture, and with infiltrations extending beyond the capsule of the node. The majority of these growths were medullary and

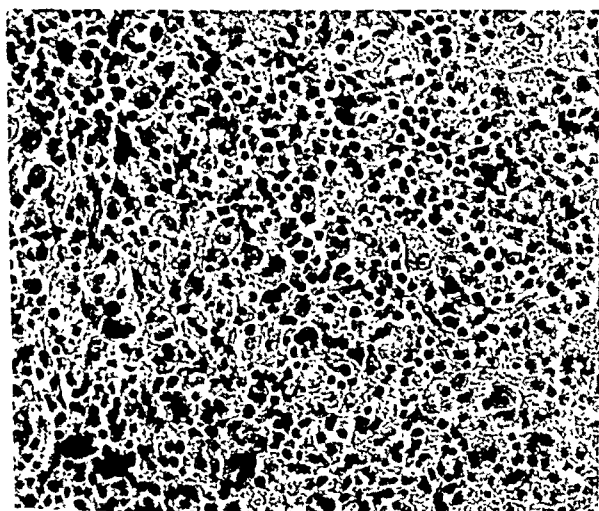


FIG. 3.—Sarcomatous Hodgkin's. Transformation into lymphoblastoma.

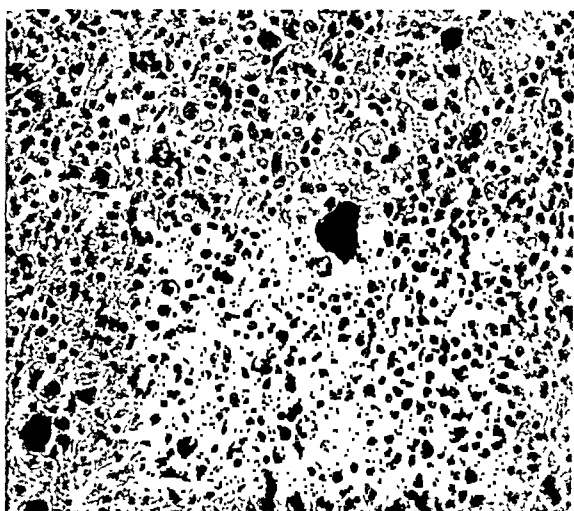


FIG. 4.—Transformation of a Hodgkin's to a lymphoblastoma. Traces of Hodgkin's foci still persistent.

showed but little stroma; in only a few was there an abundant stroma. In the latter the cells were often of the type of large lymphocytes, rather than of the small lymphocyte. The majority of these cases of lymphoblastoma showed clinically more or less febrile reaction, resembling that in the Hodgkin's cases. Similar degenerative changes (necrosis) occurred also in the enlarged nodes. Nine cases showed a transformation from the aleukæmic stage to the leukæmic. In the twenty autopsy cases of lymphatic leukæmia practically the same glandular lesions were found as in the twenty autopsy cases of aleukæmic lymphoblastoma. In both forms the kidneys usually presented large and numerous metastases, the liver showed marked lymphoblastomatous infiltrations of the periportal tissues, and the spleen showed a diffuse lymphoblastomatous metaplasia. Infiltration in the retroperitoneal adipose tissue and in the lungs also was frequent. In several cases of the large-celled form coming to autopsy emboli of large atypical cells were found in great numbers in the pulmonary, liver, splenic and renal vessels. In forty-four of the biopsy cases a diagnosis of atypical lymphoblastoma was rendered

because of combined features of Hodgkin's and lymphoblastoma, or of reticulo-endothelioblastoma and lymphoblastomatous hyperplasia. In our experience the response to X-ray irradiation of the aleukæmic form of lymphoblastoma has been on the whole much better than in the case of Hodgkin's, but even after several years of apparent disappearance of the enlarged nodes recurrence takes place with a fatal ending.

*Mycosis Fungoides*.—In the great majority of cases this disease is a small-celled lymphoblastoma involving the primitive lymph-nodes of the papillary layer of the dermis, but ultimately coalescing to form the fungoid tumors of the skin, becoming generalized at last in all of the lymphoid tissues of the body, lymph-nodes, spleen, bone-marrow and thymus, and presenting the same periportal infiltrations in the liver, and renal metastases that are characteristic of primary lymphoblastoma of the regional lymph-nodes. It also may become leukæmic, or may be associated with a leukæmia from the beginning

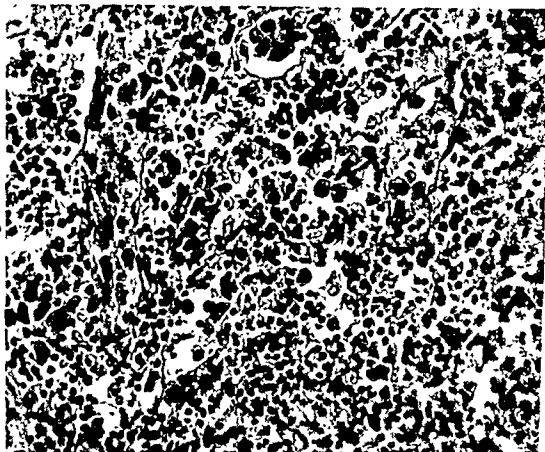


FIG. 5.—Lymphoblastomatous transformation of Hodgkin's. Biopsy two years previously showed typical Hodgkin's. Present biopsy showed complete disappearance of Hodgkin's lesion, with replacement by lymphoblastoma. Confirmed by further biopsies.

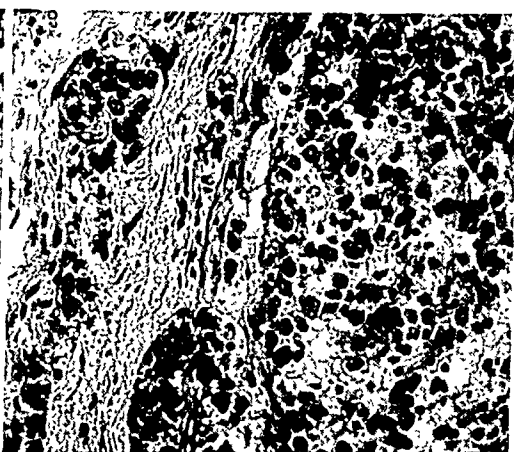


FIG. 6.—Lymphoblastomatous transformation of Hodgkin's disease. Infiltration of neoplastic process through capsular blood-vessels.

(leukæmia cutis). In one of our cases coming to autopsy the infiltrations in the skin were typically those of Hodgkin's disease; in another the cells were chiefly of the plasma-cell type; in another they were myeloid in character, while in another case the infiltrations and the skin tumors consisted chiefly of eosinophile cells, mostly mononuclears. Aside from the skin involvement, which may precede or follow that of the regional lymph-nodes, the pathologic picture is that of a generalized lymphoblastoma. When primary in the primitive lymph-nodes of the skin the development of the disease may be very slow; a "pre-mycotic stage" of several years' duration may precede the development of actual tumors in the skin. In our material there were twenty-three cases of the aleukæmic form of lymphoblastoma, and five cases showing a transformation from the aleukæmic to the leukæmic stage, while three cases were of the leukæmic cutis type from the beginning of the process. Other observers have noted the occurrence of the Hodgkin's type of lesion in the cutis, but the writer has found no reported case of the eosinophilic form. It is possible that some of the cases diagnosed clinically

as multiple hæmorrhagic sarcoma of Kaposi may be related to mycosis fungoides. In our material we have had but one biopsy from such a case, and the microscopic picture appeared indistinguishable from that of the early pre-mycotic stage of mycosis.

The above brief analysis of our material forms the foundation upon which the following conclusions are drawn:

1. Hodgkin's disease, sarcomatous Hodgkin's, aleukæmic and leukæmic lymphoblastoma, aleukæmic and leukæmic mycosis fungoides are all true neoplasms and are genetically closely related.

2. Transition forms between all of the types exist.

3. They differ chiefly in the degree of entdifferentiation shown by their cell types, and in their point of origin.

4. They all take their origin from perivascular reticulo-endothelium, or the maternal lymphoblasts of the lymphoid tissues of the body.

5. Those arising from the hæmatopoietic perivascular reticulo-endothelium take on the type of Hodgkin's, sarcomatous Hodgkin's (reticulocyto-endothelioblastoma), or even of myeloid forms of sarcoma. Those arising from the maternal lymphoblasts have the character of the lymphoblastoma, small-celled or large-celled, aleukæmic or leukæmic. The maternal lymphoblasts are derived from the same perivascular reticulo-endothelium, but represent a higher stage of differentiation than do the Hodgkin's and the reticulocyto-endothelioblastoma forms. The sarcomatous Hodgkin's of the reticulocyto-endothelioblastoma type represents a greater entdifferentiation than the Hodgkin's type; while the lymphoblastoma represents a higher stage of differentiation.

6. The more undifferentiated forms, Hodgkin's, sarcomatous Hodgkin's and typical lymphoblastoma forms occur chiefly in individuals of younger ages; while the typical aleukæmic and leukæmic neoplasms are more frequent in older individuals.

7. They all run a similar clinical course, often with fever, characterized by remissions and recurrence of the tumors, with the development of a progressive tumor cachexia, anæmia, emaciation and prostration. No case has ever been cured; when removed surgically the regenerated glands become similarly involved in the process. While suggesting analogies with chronic infectious processes, they differ from these in that no mild or cured cases occur, there is no evidence of any immune reaction on the part of the organism, and the process shows a steady malignant progression to the fatal termination.

8. Pathologically, the lesions are neoplastic in type, rather than granulomatous; they show true infiltrations and metastases. In their cell types and architecture they follow definite patterns which cannot be explained on the basis of an inflammatory reaction.

9. There is but one method of treatment, which will delay, but will not halt, the inevitable malignant progress of these growths, and that is the judicious and systematic employment of X-ray irradiation.

# STUDIES IN HODGKIN'S DISEASE

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THE idea of the tuberculous nature of Hodgkin's disease has never really been lost sight of by the students of that disease since it was first expressed by Sternberg in 1899. Ewing has always emphasized the close relationship between Hodgkin's disease and tuberculosis, which is indicated by the very similar granulomatous nature of the two processes, by the frequent finding of acid-fast bacilli in the lesions, by the rarely positive atypical reaction produced in experimental animals, and by the frequent incidence of generalized tuberculosis as a terminal manifestation in this disease. Furthermore, he points out that "tuberculosis follows Hodgkin's disease like a shadow." Subsequent to the investigation of Much, Ewing identified Gram-positive granules, and occasionally acid-fast rods in many of the lesions of Hodgkin's disease, which further strengthened his theory that the tubercle bacillus plays an important part in the etiology of this disease.

As has just been stated, the granulomatous character of the typical lesions spoke strongly in favor of this conception and the finding of the characteristic granules by Much in 1910, and the recent studies by Kahn have revived it. A strong argument in favor of this opinion was the fact that the majority of guinea-pig inoculations with Hodgkin's lesions resulted negatively with respect to tuberculosis. In other words, the tubercle bacilli that have been demonstrated in Hodgkin's nodes appear to have represented an independent infection. Therefore, it seemed to me that if Hodgkin's disease is tuberculous, and is not caused by the human or bovine variety, as evidenced by the negative animal experiments, the disease might be due to the hitherto completely ignored avian tubercle bacillus.

In the experimental animal inoculations previously reported, only guinea pigs, rabbits and monkeys had been used; that is, animals relatively insusceptible, or immune, to avian infection. As the guinea pig was the animal most frequently employed in the reported cases of experimental inoculation with Hodgkin's material, it was determined to carry on a series of preliminary experiments to test the resistance of this animal to avian infection, and to find out whether an increased susceptibility could be produced by the previous inoculation of heterologous strains of tubercle bacilli.

For this purpose one series of animals was inoculated with live avian tubercle bacilli. A second series was treated with killed human tubercle bacilli before inoculation with the live avian organisms, and a third group received killed bovine bacilli as a preliminary injection before inoculation with the live avian bacilli.

## STUDIES IN HODGKIN'S DISEASE

It was found, as the result of these experiments, that guinea pigs have a natural resistance to avian infection, shown by the long period of incubation, six to eighteen months, before generalization of the disease. The lesions developed also differed from those usually seen in animals inoculated with human tuberculosis, in that they seemed to have a predilection for the lymphatic system, shown by the extensive involvement of all nodes; cervical, axillary, mediastinal and bronchial, with less significant, although sometimes extensive, lesions in the liver, lungs and spleen.

The nodes, on microscopic examination, revealed the characteristic Sternberg-Reed histology.

These observations seemed to establish the fact that guinea pigs, although relatively insusceptible to avian infection, nevertheless occasionally develop a delayed and atypical tuberculosis and suggest that the preliminary inoculation of guinea pigs with killed human bacilli renders them less resistant to avian infection.

Furthermore, these findings offer an explanation for the negative or delayed positive inoculations obtained in the reported experimental inoculations of guinea pigs with Hodgkin's lesions. They also answer a strong objection to my thesis, which I encountered early in my study, namely, that the avian tubercle bacillus is not pathogenic for mammals.

On the strength of these results, I concluded that the simplest way to determine whether Hodgkin's disease was at all related to the avian tubercle bacillus, was to inoculate birds with Hodgkin's lesions, an experiment which, so far as could be ascertained, had never been reported.

Therefore, in November, 1926, I undertook a series of experiments on chickens to test this theory.

Five healthy chickens were inoculated intravenously with emulsions of lymph-nodes from two cases of clinically and histologically characteristic Hodgkin's disease.

All of these chickens developed either a typical or an atypical tuberculosis, and in the tissue smears, stained by Ziehl-Nielsen method, acid-fast granules and rods, extra- and intracellular, were demonstrated in two of them, and non-acid-fast granules in another.

Re-inoculation of material from the lesions of one of these chickens into another chicken produced an identical, though more extensive, manifestation of the disease.

An atypical tuberculosis developed in guinea pigs after inoculation of the tissue from the fourth chicken. A growth of bacteria with the staining and cultural characteristics of the avian tubercle bacillus was produced on egg media from material from this guinea pig.

Cultures from these birds on egg media were contaminated in all instances. In one the chicken culture gave a symbiotic growth of a blastomyces-like organism with an acid-fast bacillus.

While it was recognized that the two short series of experiments here reported could not quite exclude the apparently unlikely alternative explana-



tion that we were dealing with an accidental avian infection, the findings seemed to justify the conclusion that in these chickens, a lesion with the histological features of Hodgkin's granuloma and comparable to avian tuberculosis had been produced after the inoculation of emulsified Hodgkin's nodes. This might indicate that the etiological agent in certain forms of Hodgkin's disease is pathogenic for birds, or that the *avian tubercle bacillus* is a factor in producing some of the lesions which are interpreted as Hodgkin's disease.

This evidence could not be considered conclusive on account of the small number of experiments, and the lack of *pure culture* of that organism from the inoculated birds. However, since that time I have studied four other cases, which confirm the previous findings and include the successful isolation of an acid-fast bacillus possessing some of the cultural characteristic of the avian tubercle bacillus. One of these cases, submitted to me from the Memorial Hospital, was the rather rare form of Hodgkin's granuloma, known as Pel Ebstein's disease, in which the gradual splenic enlargement with intermittent attacks of fever are the most prominent features, the associated lymph-node involvement being either absent or insignificant.

The histological study suggested the presence, mainly in the spleen, of an atypical Hodgkin's disease, the lesions consisting almost entirely of focal necrosis. Direct smears from spleen stained by Ziehl-Nielsen's method showed a few acid-fast bacilli, and cultures on egg media gave a scant growth resembling the avian type of tubercle bacillus. The fresh macerated splenic tissue was inoculated into four chickens, one rabbit intravenously, one rabbit subcutaneously, and also into four guinea pigs, two of which were previously treated and two normal ones. One of the chickens was accidentally killed four months after injection. The other three lived from six to twelve months. All of these birds, at autopsy, showed lesions of avian tuberculosis in liver and spleen, with typical Sternberg-Reed histology. Acid-fast organisms were found in direct smears and in stained sections. Cultures on egg media from the liver and spleen of these chickens showed a growth similar to that obtained from the original splenic material; the rabbit inoculated intravenously died of acute septicæmia twenty days after injection; and cultures on egg media gave a growth with the characteristics of the avian tubercle bacillus. Re-inoculation intravenously into a second rabbit produced similar lesions, and positive cultures of tubercle bacilli were recovered.

The rabbit inoculated subcutaneously lived six months and the autopsy revealed typical generalized tuberculosis.

Of the four guinea pigs injected, the two previously treated with killed human tubercle bacilli died about eleven months after injection, with extensive lymph-node tuberculosis. The other guinea pigs are still alive, twenty-two months after inoculation.

The findings in this case seem to be of value in offering evidence of the avian tuberculous nature of a condition which presents a histological relationship to typical Hodgkin's disease and indicates that in the human being.

as well as in the lower animal, avian infection may be exhibited in various pathological lesions.

Another case was one of Hodgkin's disease in a child of eight years, in which the prominent symptoms were generalized involvement of cervical mediastinal bronchial and retroperitoneal lymph-nodes with enlargement of the spleen.

Biopsy of the nodes showed the typical histology of Hodgkin's disease, and this histological diagnosis was confirmed at autopsy.

Emulsified material from these nodes was inoculated into two treated guinea pigs, intravenously into two normal chickens and one rabbit subcutaneously. All of these experimental animals, except the rabbit, developed tuberculosis, and positive tubercle cultures on egg media were obtained from the lesion.

This study permits the conclusion that Hodgkin's disease may represent an atypical tuberculosis, possibly avian in type.

A recent case may be added to this group:

A young man of twenty-seven years had had his tonsils and right cervical lymph-nodes removed in 1920, and enlarged cervical and axillary nodes removed in 1927. At both of these operations the histologic diagnosis was tuberculosis and the patient's recovery prompt. Four months before his death he had a chill, following exposure, and developed pneumonia. He recovered in three weeks, but after this had a persistent afternoon temperature, usually between 100 and 101 degrees. When admitted to the hospital, he had enlarged lymph-nodes in both sides of the neck, and the X-ray diagnosis was consistent with the autopsy findings. The sputum was negative for tubercle bacilli on ten occasions.

The post-mortem examination revealed massive lymphoma of thoracic and abdominal lymph-nodes with extension into the liver and spleen. These lesions were associated with hydrothorax, hydropericardium, ascites, and recent acute endocarditis. The latter consisted of delicate, but firm, yellow vegetations, along the line of closure of the mitral valve and a few vegetations on the aortic valve.

The microscopic examination of the nodes showed the typical Sternberg-Reed histology.

Emulsified material from the nodes was inoculated intravenously into two chickens, subcutaneously into four guinea pigs and one rabbit. One of the chickens died within a few days after injection before any typical lesions could develop. The second bird lived ten months and at autopsy showed extensive tuberculosis of liver and spleen.

Of the four injected guinea pigs, one lived six months; another eleven months; and at autopsy both of these animals showed generalized tuberculosis, involving extensively the lymph-nodes and bones.

Cultures from the lesions on egg media produced a growth of acid-fast bacilli with the cultural features of the avian strain of tubercle bacilli.

The remaining two guinea pigs are still alive, eighteen months after inoculation, which speaks strongly in favor of an avian tubercle infection. The rabbit lived eleven months and the autopsy revealed a peculiar nodular tuberculosis of liver and mesenteric nodes.

The experimental and cultural evidence obtained in this case further strengthens the theory that the characteristic histological picture of Hodgkin's disease is found as the result of infection with the avian strain of tubercle bacilli.

*Discussion.*—These accumulated data seem to justify the conclusions that many of the recorded cases of Hodgkin's granuloma are atypical tuberculosis and that if the experimental animal inoculations of such material were pursued consistently along the lines of recent investigation it would determine the nature of at least one form of clinical Hodgkin's disease.

Furthermore, the results obtained in the case previously reported, of Pel Ebstein's type of Hodgkin's disease, confirms the theory of the tuberculous origin of this disease and suggests the etiological factor to be the avian type of tubercle bacillus.

Having become convinced that the avian tubercle bacillus was the

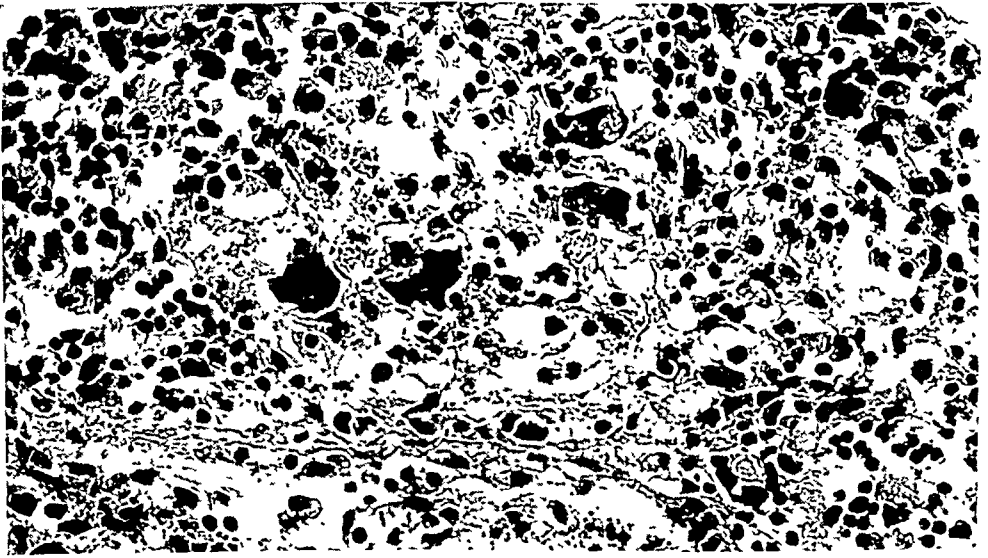


FIG. 1.—Case III.

etiological agent in certain forms of Hodgkin's granuloma, it seemed logical that reactions, analogous to those observed with Koch's old tuberculin, could be obtained by testing cases of Hodgkin's disease with avian tuberculin.

This supposition was further strengthened by the reported observations of Lowenstein and others, that avian tuberculin is specific for avian tuberculosis and does not react to human or bovine infection.

Therefore, a standard tuberculin was made from glycerin broth culture of avian tubercle bacilli, and cutaneous tests with avian tuberculin on cases of suspected Hodgkin's disease were carried on. The technic was the same as with Koch's old tuberculin and both the Mantoux and von Pirquet methods were used.

Seven cases from the Cornell Clinic were tested. Of these four had lymphadenopathy, either generalized or localized in the cervical region. In two of these four cases biopsy showed the typical histology of human tubercu-

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losis and they gave a negative avian reaction with a strongly positive old tuberculin test. One of the remaining two cases, with generalized lymphadenopathy, had a blood picture of leukæmia, and the test was negative. The fourth case had a single suppurating axillary node and smaller nodules in the skin with extensive involvement of scapula. As no biopsy could be obtained, the probable clinical diagnosis was sarcoma. The avian tuberculin test was negative.

A fifth case proved, on histological examination, to be a lymphosarcoma, and gave a negative avian tuberculin reaction.

The remaining two cases were particularly interesting in that they both were unusual forms of Hodgkin's disease. One of them gave a history of recurring attacks of chills and fever over a period of eighteen months, associated with enlargement of cervical axillary and inguinal nodes.

Histological examination of inguinal node revealed fibrosis, no necrosis or typical tubercles with an occasional myeloid giant cell. This was unconvincing, but it is a well-known fact that inguinal nodes are unsatisfactory for biopsy examination, for the reason that so much fibrosis usually exists that the true character of the lesion cannot be determined. Avian tuberculin tests were strongly positive. Old tuberculin tests were less positive.

The other case was a rare form of Hodgkin's disease of the skin with associated involvement of cervical and axillary nodes. The lesions both in the skin and lymph-nodes gave the histological picture of Hodgkin's granuloma. A positive reaction to avian tuberculin was obtained and a less marked one to Koch's old tuberculin.

Five cases of suspected Hodgkin's disease have been tested with avian tuberculin at the New York Hospital.

In two of the cases which occurred in children, the biopsy diagnosis was atypical tuberculosis. Both of them gave strongly positive avian and Koch old tuberculin tests—the avian, however, much more pronounced than the human.

Of the three remaining cases, one showed extensive involvement of cervical and mediastinal lymph-nodes. In the other, the abdominal nodes were the distinctive lesion. These two cases histologically were diagnosed as atypical Hodgkin's disease, or possibly lymphosarcoma. In both of them the avian tuberculin reaction was strongly positive, the reaction to human tuberculin less definite.

The remaining case proved to be a thyroglossal cyst, and in this also a positive avian tuberculin reaction was obtained.

Recently a voluntary communication was received from Doctor Woolley of the Loomis Sanatorium in which he reported a positive avian and a negative human tuberculin reaction in a case of Hodgkin's disease, in which the diagnosis was verified by histological examination.

The findings in this short series of avian tuberculin skin tests, although suggestive, are not convincing. In twelve cases of suspected Hodgkin's disease, positive avian tuberculin reactions were obtained in seven of them.

Four of these were histologically characteristic of Hodgkin's disease. Of three remaining, two showed atypical tuberculosis on microscopic examination of the nodes, and the third was a thyroglossal cyst of the neck. (The most reasonable explanation for the positive avian tuberculin reaction in this last case seems to be the presence of a latent, or healed avian infection.)

Five of the twelve cases were negative to avian tuberculin. On histological examination, two of these proved to be typical human tuberculosis, one a lymphosarcoma, another a sarcoma of the scapula. In the fifth, the microscopic picture was not characteristic of Hodgkin's disease, but more nearly approached that of a lymphosarcoma.

The fact that in many cases both the cutaneous test with old tuberculin and with avian tuberculin are positive, raises the question of the specificity of these reactions. Lowenstein and others believe that the two reactions are specific, that is, each dependent on a separate infection by the respective microorganism.

However, from our experience with this limited number of cases, we are not impressed with the specificity of the avian tuberculin reaction in Hodgkin's disease, but it is possible that the specificity may depend on some hitherto undetermined factor inherent in the microorganism, and with this in mind further investigations are now being carried out to determine, if possible, the nature of this specific antibody.

This summary of my studies is presented in considerable detail in order to show that the accumulated evidence presents substantial proof of the etiological significance of the avian tubercle bacillus in certain clinical forms of Hodgkin's disease.

It is peculiarly gratifying to me to record that the inspiration for this study was derived directly from the influence of Doctor Ewing's concept of the tuberculous nature of Hodgkin's disease.

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# THERAPY OF SPONTANEOUS MOUSE CANCER

FAILURE OF TUBERCULIN, KARKINOLYSIN, AND SOME  
INORGANIC COMPOUNDS THEREIN

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WE HAVE previously used groups of dyes and other organic compounds derivable from coal tar in the search for clues to therapy of the spontaneous mammary tumor in mice.<sup>1</sup> In these papers reasons are given for attempting work so little promising. The later paper contains citations to the literature.<sup>2</sup> These lead to the chief contributions covering the attempts at therapy of animal cancer.

While we believe all chemical elements in their simplest available forms should be proved with respect to possible influence on animal cancer, the rather miscellaneous group of inorganic compounds here considered was chosen for a more specific reason. Nearly all of them, or similar compounds, have been shown by Ishiwara<sup>3</sup> to exhibit in various degrees a tendency to inhibit the growth or cause degeneration of the transplanted tumor in mice. He divided the elements concerned into four ascending groups based on their effectiveness. The first, whose twenty-two elements had no effect, nevertheless contains seven which various workers have at times recognized as tumor inhibiting. The next two groups contain respectively twelve and seventeen elements. The fourth group, showing most unequivocal effect, consisted of six; caesium, germanium, selenium, cerium, scandium and ytterbium. All these elements, and especially those of the last group, demanded further investigation with respect to their effect on cancer, since they influenced propagable tumors in a way which might be useful therapeutically. Nevertheless, having in mind the lability of propagated tumors in general, we were not optimistic that Ishiwara's results would hold for spontaneous growths.

The recent interest in the relation of cancer to tuberculosis, and the use of tuberculin in advanced cases of human cancer, led us to look to animal cancer for some basis for a tuberculin therapy. The treatment being experimental, with human patients only cases far advanced and of the worst prognosis are selected, and the dangers of the tuberculin itself require conservative dosage. From an experimental standpoint the use of mice gave important advantages in that large doses could be given, very early growths treated, and the treatment continued intensively over long periods.

*The Inorganic Compounds.*—Most of the materials were supplied by the American market and were in every case of the highest purity obtainable. We are highly indebted to Professor B. S. Hopkins, of the University of Illinois, for salts of the rare earths samarium, neodymium, lanthanum and

yttrium. The first three of these were unobtainable in the market. We could find no source of supply for the desired ytterbium, and substituted for it the closely related samarium and neodymium. The scandium salt used was purchased from Adam Hilger, Ltd., of London, being a highly purified product prepared by Sir William Crookes. The columbium salt was furnished through the kindness of Dr. C. W. Balke, of the Fansteel Products Company.

Our aim was to repeat with spontaneous tumors those therapeutic applications of Ishiwara in which he reported some success with transplanted tumors. Of the thirty-five elements which he names in this connection we have used thirty-three—all except ytterbium and iridium. In addition, samarium neodymium, lanthanum and thorium have been tested.

*Tuberculin.*—The evidence is that the tuberculins, whether preparations of the bacilli themselves, or the filtrates of cultures, are not toxic to normal animals. Our experiments confirm this. Certainly the normal mouse will endure enormous doses. We have not used the large amounts of material necessary to bring about obviously toxic effects. A single dose of fifteen milligrams of an emulsion of bacilli (B. E.), two-thirds of which entered intravenously, followed by nine milligrams more subcutaneously four days later, did not obviously affect a normal male mouse of nineteen grams' weight. As for filtrate 347, and the bovine filtrate, the tabulations show what large amounts may be given daily with impunity. Here the question is left without finding a toxic or lethal dose if such exist in any proper sense. Manifold larger doses would probably be endured. Thus, while we have administered relatively great quantities to very small animals not only free of tuberculosis but little if at all susceptible to it, the experiments do not cover the limiting cases of maximum dosage. Special concentrates would be required.

"Filtrate 347," prepared at the Johns Hopkins Hospital under the direction of Dr. Alan Krause, was furnished us through the helpful courtesy of Dr. Alan C. Sutton, of Baltimore. It is a bouillon filtrate, without preservative, identical with that used experimentally on human cancer patients at the Johns Hopkins Hospital.

Tuberculin B.E. is in the form of dry tablets prepared by Parke, Davis and Company. They consist of dried human and bovine tubercle bacilli, in approximately equal parts, disintegrated by grinding, and mixed with a soluble base. A suspension of the bacillary fragments in distilled water was injected.

Tuberculin T.R. consists of similar tablets prepared by Parke, Davis and Company, from human and bovine tubercle bacilli in approximately equal parts. The bacilli are washed thoroughly in water, ground and mixed with a soluble base. A suspension was injected.

Tuberculin B.F. (Bovine) is a bouillon filtrate made by Parke, Davis and Company. It is preserved with 0.5 per cent. phenol. It was received in and used from one-cubic-centimetre rubber-capped glass bulbs.

Karkinolysin (Hanson) is "a thymic extract, each cubic centimetre representing 0.6 gram of the fresh gland. Average dose one cubic centimetre intramuscularly, once daily. For experimental use only."

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*Technic. Explanation of Tables.*—The methods were in general the same used in previous work. The solutions were all made with distilled water. The single sample of filtrate 347 was kept carefully aseptic and near the freezing point, and the daily portion was aspirated from a vaccine bottle through the rubber diaphragm stopper, which was never removed. Karkinolysin was handled in the same way. The rest of the material required no especial precautions. No rigid asepsis was used with the injections into mice.

The tumor used was the mammary adenocarcinoma in the albino mouse, spontaneous in every case. Injections were often continued almost to the death of the animal, and far beyond a stage where regression seemed possible. The terminal cachexia was often accompanied by a shrinkage of the tumor. Where the maximum size of the latter did not occur at end of treatment or at death, it is indicated in the last column, as is the development of a second tumor during treatment.

For the inorganic compounds it was aimed to give as high a dose as could be continued daily for a long period without loss of body weight. Every chemical therefore has been used at or near the maximum dosage. In

TABLE I

## *Inorganic Compounds*

- |   |                                     |
|---|-------------------------------------|
| 1. Ammonium vanadate                                | 29. Potassium bifluoride            |
| 2. Antimony potassium tartrate                      | 30. Potassium borotartrate          |
| 3. Arsenic pentoxide                                | 31. Potassium columbium oxyfluoride |
| 4. Beryllium carbonate                              | 32. Potassium fluosilicate          |
| 5. Bismuth potassium iodide                         | 33. Rubidium chloride               |
| 6. Boric acid                                       | 34. Rubidium hydroxide              |
| 7. Cadmium acetate                                  | 35. Ruthenium chloride              |
| 8. Cæsium aluminum sulphate                         | 36. Samarium nitrate                |
| 9. Cæsium chloride                                  | 37. Scandium potassium sulphate     |
| 10. Ceric sulphate                                  | 38. Selenious acid                  |
| 11. Cerous chloride                                 | 39. Silicic acid                    |
| 12. Cerous oxalate                                  | 40. Sodium fluoride                 |
| 13. Cerous sulphate                                 | 41. Sodium selenate                 |
| 14. Cobaltous iodide                                | 42. Sodium silicate                 |
| 15. Cobaltous chloride                              | 43. Sodium tellurite                |
| 16. Germanium dioxide                               | 44. Sodium vanadate                 |
| 17. Gold sodium chloride                            | 45. Stannic chloride                |
| 18. Hexammincobalt chloride (Luteo-cobalt chloride) | 46. Strontium chloride              |
| 19. Indium trichloride                              | 47. Telluric acid                   |
| 20. Iron chloride (ic)                              | 48. Thorium nitrate                 |
| 21. Iron salicylate                                 | 49. Titanium potassium oxalate      |
| 22. Lanthanum nitrate                               | 50. Uranyl nitrate                  |
| 23. Neodymium nitrate                               | 51. Uranyl chloride                 |
| 24. Palladium chloride                              | 52. Vanadium chloride               |
| 25. Palladium sodium chloride                       | 53. Yttrium nitrate                 |
| 26. Phosphoric acid (meta)                          | 54. Yttrium nitrate (Hopkins)       |
| 27. Phosphorous acid                                | 55. Zinc acetate                    |
| 28. Platinic acid, chloro-                          | 56. Zirconium nitrate               |
|   | 57. Zirconium oxychloride           |



TABLE II  
*Inorganic Compounds*

| Serial | Per cent.<br>of solute | Dose—<br>mg. or ml | No. of doses |              | Duration—<br>days | Survival—<br>days | Total<br>dosage—<br>mg. | Weight of mouse—gm |                |                | Diameter of tumor—mm |               |              | Remarks  |
|--------|------------------------|--------------------|--------------|--------------|-------------------|-------------------|-------------------------|--------------------|----------------|----------------|----------------------|---------------|--------------|--|
|        |                        |                    | Intrav.      | Subc.        |                   |                   |                         | Begin-<br>ning     | End            | Death          | Begin-<br>ning       | End           | Death        |  |
| 1      | 0.5<br>0.5             | 1<br>0.5           | 53           | 23<br>4      | 23<br>57          | 29<br>58          | 2.3<br>2.8              | 33<br>22           | 30<br>23       | 24<br>20       | 11<br>7              | 15<br>16      | 14<br>15     |  |
| 2      | 1<br>1                 | 1<br>1             | 19<br>16     | 6<br>25      | 25<br>41          | 26<br>103         | 25<br>41                | 28<br>25           | 26<br>26       | 26<br>21       | 13<br>9.             | 16<br>12      | 16<br>13.5   | Maximum 19 mm<br>A second tumor arose          |
| 3      | 0.625                  | 0.625              | 76           | 12           | 88                | 89                | 5.5                     | 28                 | 27             | 27             | 8                    | 16            | 16           |  |
| 4      | Sat.                   | 5 ml               | 27           | 16           | 43                | 49                |                         | 31                 | 33             | 24             | 8                    | 25            | 21           |  |
| 5      | 2                      | 5                  | 4            | 26           | 30                |                   | 150                     | 28                 | 28             |                | 9                    | 14            |              | Surviving.                                     |
| 6      | Sat<br>4<br>4          | 2 ml<br>12<br>12   | 53<br>74     | 3<br>34<br>3 | 56<br>34<br>77    | 106<br>35<br>79   | 108<br>924              | 31<br>29<br>26     | 34<br>28<br>27 | 31<br>28<br>24 | 6.5<br>4<br>9.5      | 23<br>9<br>28 | 28<br>26     | A second tumor arose<br>Three tumors All grew. |
| 7      | 1                      | 25                 | 12           | 9            | 21                | 22                | 5.25                    | 29                 | 23             | 23             | 9                    | 11            | 11           |  |
| 8      | 5<br>0.5               | 5<br>0.5           | 11<br>28     | 43<br>48     | 54<br>78          | 56                | 27<br>3.9               | 27<br>26           | 25<br>27       | 22             | 9<br>7.5             | 13<br>18.5    | 13           |  |
| 9      | 2.5                    | 5                  | 36           | 1            | 37                |                   | 185                     | 28                 | 23             |                | 8.5                  |               | 15           | Surviving.<br>Maximum 17 mm                    |
| 10     | Sat<br>0.1             | 2 ml.<br>0.1       | 34<br>25     | 5<br>6       | 39<br>33          | 50<br>35          | 31                      | 27<br>27           | 31<br>18       | 27<br>16       | 10<br>6.5            | 29<br>7       | 32<br>7      |  |
| 11     | 0.5<br>0.5             | 1<br>0.5           | 29<br>21     | 22<br>16     | 52<br>37          | 78<br>39          | 5.1<br>1.8              | 30<br>28           | 35<br>21       | 37             | 7.5<br>11            | 33<br>16      | 37.5<br>13.5 |  |
| 12     | 0.5                    | 25                 | 15           | 32           | 47                | 53                | 11.7                    | 36                 | 31             | 31             | 10                   | 19            | 19           |  |
| 13     | 25<br>25               | 25<br>125          | 34           | 21<br>14     | 21<br>50          | 22                | 5.25<br>6               | 32<br>30           | 27             | 25             | 13<br>7              | 17<br>17      | 16           |  |
| 14     | 25<br>25               | 5<br>5             | 22           | 58<br>61     | 58<br>83          | 63<br>84          | 27<br>11.5              | 29<br>26           | 25<br>23       | 18<br>21       | 14.5<br>6            | 23.5<br>11.5  | 21<br>10     |  |
| 15     | 135                    | .135               | 35           | 33           | 68                | 69                | 9.1                     | 26                 | 23             | 20             | 7                    | 12.5          | 12.5         | Missing  |
| 16     | 2<br>Sat               | 4<br>1 ml.         | 14<br>15     | 47<br>9      | 62<br>24          | 97<br>26          | 24.8                    | 29<br>31           | 27<br>30       | 28<br>25       | 19<br>10             | 27.5<br>16    | 27<br>14     |  |

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|    |      |        |    |    |    |     |      |    |    |    |      |      |                       |
|----|------|--------|----|----|----|-----|------|----|----|----|------|------|-----------------------|
| 17 | .025 | .05    | 10 | 27 | 46 | 93  | 2 3  | 27 | 29 | 21 | 11.  | 17.  | 21.                   |
|    | .025 | .05    | 48 | 14 | 62 | 63  | 3.1  | 30 | 24 |    | 5.5  | 11 5 |                       |
| 18 | .05  | .05    | 46 | 2  | 48 | 50  | 2 4  | 29 | 24 |    | 13.  | 18 5 | 18.5                  |
| 19 | .03  | .03    | 21 | 19 | 40 | 41  | 1.2  | 27 | 28 |    | 9 5  | 15.  | 15.                   |
| 20 | .009 | .009   | 15 | 26 | 41 | 119 | 36   | 29 | 28 | 21 | 9    | 16.  | 19                    |
| 21 | 2 5  | 5      |    | 34 | 34 | 61  | 170  | 28 | 29 |    | 6.   | 12   | 19                    |
| 22 | .04  | .04    | 21 | 58 | 70 | 80  | 3 16 | 23 | 21 | 19 | 6    | 14 5 |                       |
|    | .006 | .006   | 35 | 12 | 47 | 49  | 28   | 27 | 18 | 18 | 5    | 10   |                       |
| 23 | 2    | 2      | 20 | 23 | 43 | 45  | 8 6  | 28 | 22 | 21 | 6    | 17   | Maximum 19 mm.        |
| 24 | .25  | 5      |    | 44 | 46 |     | 22   | 25 | 21 |    | 4    | 7    | Surviving.            |
|    | Sat. | 1 ml.  |    | 24 | 24 | 24  |      | 28 | 25 | 25 | 9    | 11   | Surviving.            |
| 25 | 1    | 4      | 3  | 27 | 30 | 20  | 12   | 28 | 25 | 18 | 4 5  | 6    |                       |
|    | 1    | 3      | 3  | 14 | 17 |     | 5 1  | 30 | 24 |    | 1    | 6    | 5 5                   |
| 26 | .4   | 4      | 35 | 44 | 88 | 89  | 31 6 | 25 | 24 | 22 | 6    | 10   | A second tumor arose. |
| 27 | 5    | 5      | 17 | 28 | 45 | 46  | 22 5 | 29 | 25 | 25 | 15 5 | 12 5 | Maximum 24 mm.        |
|    | 5    | 5      | 11 | 30 | 41 | 42  | 20 5 | 29 | 24 |    | 7 5  | 10 5 |                       |
| 28 | .05  | 1      | 17 | 44 | 62 | 72  | 6 1  | 26 | 27 |    | 8 5  | 16   | 17                    |
| 29 | 1    | 5      | 22 | 11 | 33 | 53  | 16 5 | 28 | 29 | 23 | 9    | 23   |                       |
| 30 | Sat. | 25 ml. | 20 | 13 | 33 | 40  |      | 27 | 27 | 18 | 10   | 18   | 15                    |
| 31 | .1   | 1      |    | 44 | 44 |     | 4 4  | 28 | 30 |    | 7 5  | 27   | Missing.              |
|    | .05  | 1      | 31 | 24 | 55 | 63  | 5 5  | 24 | 24 |    | 6    | 17 5 | 17 5                  |
| 32 | .1   | 1      | 44 | 32 | 78 |     | 7 6  | 29 | 25 |    | 4    | 7 5  | Surviving.            |
| 33 | 1.   | 4      | 40 | 71 | 72 | 128 | 28 4 | 25 | 30 | 36 | 7    | 15   |                       |
|    | 1.   | 4.     |    | 22 | 64 | 130 | 24 8 | 32 | 31 | 25 | 6    | 13.  | 27                    |
| 34 | .6   | 6      | 12 | 25 | 37 | 38  | 22.  | 23 | 24 | 24 | 10.  | 23 5 | 23 5                  |
| 35 | .01  | .03    | 29 | 12 | 41 | 58  | 1 2  | 26 | 28 | 23 | 7 8  | 20   | 22                    |
| 36 | .5   | .5     | 16 | 20 | 36 | 37  | 18   | 29 | 22 | 19 | 7 5  | 12 5 | 11                    |
|    | .5   | .5     | 9  | 34 | 43 | 44  | 21 5 | 27 | 26 | 24 | 11.  | 15   | 14                    |
|    | .05  | .05    | 40 | 15 | 55 | 56  | 2 75 | 25 | 25 | 22 | 11.  | 24 5 | 22 5                  |
| 37 | .1   | .2     | 12 | 40 | 52 | 53  | 10 4 | 25 | 25 | 22 | 9 5  | 14   | 14.                   |
|    | .1   | .1     | 21 | 45 | 66 | 67  | 6 6  | 31 | 29 | 27 | 7    | 10   | 10                    |
|    | .01  | .01    | 31 | 23 | 54 | 55  | 54   | 26 | 31 | 30 | 9    | 33   | 33                    |

# SIMPSON AND MARSH

TABLE II (Continued)

| Serial | Per cent.<br>of solute | Dose—<br>mg or ml | No. of doses |       | Duration—<br>days | Survival—<br>days | Total<br>dosage—<br>mg. | Weight of mouse—gm. |     |       | Diameter of tumor—mm. |      |       | Remarks                        |
|--------|------------------------|-------------------|--------------|-------|-------------------|-------------------|-------------------------|---------------------|-----|-------|-----------------------|------|-------|--------------------------------|
|        |                        |                   | Intrav.      | Subc. |                   |                   |                         | Begin-<br>ning      | End | Death | Begin-<br>ning        | End  | Death |                                |
| 38     | .025                   | .05               | 25           | 24    | 49                | 57                | 2 4                     | 31                  | 29  | 21    | 11                    | 14 5 | 12 5  |                                |
| 39     | .1                     | .2                | 32           | 1     | 40                | 43                | 6 6                     | 25                  | 23  | 21    | 9                     | 15.  | 15 5  |                                |
| 40     | .5                     | 5                 | 29           | 15    | 44                | 47                | 22                      | 30                  | 22  | 20    | 8                     | 15 5 | 12.   |                                |
|        | .5                     | 5                 |              | 37    | 38                | 40                | 18 5                    | 28                  | 22  | 22    | 7                     | 10   |       |                                |
| 41     | .1                     | 1                 | 44           | 27    | 73                | 74                | 7 1                     | 25                  | 20  | 19    | 7.                    | 19   | 17 5  |                                |
| 42     | 1                      | 2 5               | 15           | 18    | 33                | 109               | 82 5                    | 29                  | 30  | 37    | 11 5                  | 25   | 40.   |                                |
| 43     | .025                   | .05               | 32           | 12    | 44                | 114               | 2 2                     | 27                  | 28  | 24    | 10                    | 16   | 26    | Maximum 11 mm.                 |
|        | .025                   | .05               | 36           | 8     | 44                | 99                | 2 2                     | 25                  | 25  | 24    | 9 5                   | 10   | 10    |                                |
| 44     | 1                      | 1                 | 49           |       | 49                | 50                | 4 75                    | 25                  | 24  | 23    | 7.5                   | 12.  | 11.   | A second tumor arose.          |
|        | 1                      | 1                 | 22           |       | 22                | 66                | 2                       | 27                  | 28  | 23    | 12.                   | 16.  | 23.   |                                |
| 45     | .1                     | 2                 | 10           | 17    | 27                | 29                | 5 4                     | 27                  | 23  | 21    | 7.                    | 8 5  | 7 5   | A second tumor arose.          |
|        | 1                      | 1                 | 23           | 45    | 70                | 71                | 6 8                     | 26                  |     | 21    | 9.                    | 17.  | 15 5  |                                |
| 46     | 2 5                    | 5.                | 18           | 14    | 32                | 34                | 160                     | 25                  | 28  | 24    | 10.                   | 22.  | 21.   |                                |
| 47     | 2                      | .05               | 64           | 41    | 105               | 106               | 5 25                    | 27                  | 23  |       | 8 5                   | 16 5 |       |                                |
| 48     | .1                     | .05               | 17           | 43    | 60                |                   | 3                       | 30                  | 31  |       | 10.                   | 20.  |       |                                |
| 49     | 1                      | 5                 | 16           | 23    | 39                | 73                | 19 5                    | 30                  | 30  | 26    | 10                    | 15 5 | 24    | A second tumor arose.          |
|        | 125                    | 25                | 17           | 3     | 20                | 24                | 5.                      | 23                  | 19  | 16    | 8 5                   | 10   | 8 5   |                                |
| 50     | .1                     | 1                 | 20           | 33    | 54                | 56                | 5 3                     | 29                  | 25  | 19    | 8.                    | 13 5 | 13    | Maximum 14 5 mm.<br>Surviving. |
|        | .01                    | .01               | 49           | 27    | 78                |                   | .76                     | 29                  | 34  |       | 7                     | 29.  |       |                                |
| 51     | .125                   | .125              | 18           | 4     | 22                | 108               | 2 7                     | 30                  | 29  | 26    | 7                     | 11.  | 26    | A second tumor arose.          |
| 52     | .125                   | .125              | 15           |       | 15                |                   | 1.8                     | 29                  | 28  |       | 5                     | 6.   |       | Surviving.                     |
| 53     | .75                    | .75               |              | 35    | 35                | 54                | 26 25                   | 28                  | 32  | 23    | 18                    | 20.  | 26    |                                |
|        | .1                     | 1                 | 15           | 21    | 36                | 37                | 3 6                     | 25                  | 24  | 21    | 5 5                   | 13.  | 13    |                                |
| 54     | .25                    | .25               | 21           | 24    | 47                | 48                | 11 25                   | 28                  |     | 20    | 7 5                   | 14   | 14    |                                |
| 55     | .05                    | .05               | 52           | 12    | 64                | 85                | 3 2                     | 32                  | 32  | 25    | 7.                    | 16.  | 16.   |                                |
| 56     | .2                     | 2                 | 8            | 56    | 64                | 76                | 12 8                    | 28                  | 31  | 28    | 8.                    | 21 5 | 21 5  | A second tumor arose.          |
|        | .2                     | .4                |              | 39    | 39                | 41                | 15 6                    | 29                  | 24  | 23    | 13.                   | 23   | 23    | A second tumor arose.          |
| 57     | 125                    | .125              | 4            | 52    | 56                | 57                | 7                       | 24                  | 27  | 22    | 10                    |      | 15 5  | Maximum 19 mm.                 |

## THERAPY OF SPONTANEOUS MOUSE CANCER

addition some mice have been treated with greatly diluted doses. The injections were intravenous when and as long as possible; daily, with some few lapses. With very few exceptions each agent has been tested against a tumor in its earlier stages, of diameter ten millimetres or less. In addition some advanced tumors have been used. Over 270 tumor mice have been sacrificed to the investigation. From these typical cases have been selected for tabulation in detail.

The inorganic compounds are listed alphabetically and numbered serially in Table I. Table II refers by serial number to this list. Each line represents one animal. Based on the anhydrous salt, the percentage of the solute is stated and the dose in milligrams of the solute. From these the volume injected, commonly 0.1 millilitre, may be reckoned. For the few saturated solutions the dose is given in millilitres and the total dosage not carried out. "Duration" means the interval between the first and last doses; "survival," the interval from first dose to death of animal. Other headings explain themselves. In a few cases, on account of slight toxicity or solubility, saturated solutions were used, the exact content undetermined; and in a few others, where a precipitate remained, as by hydrolysis, the solution was shaken and a uniform suspension included in the injection. The doses of iron salicylate, not appreciably soluble, represent merely subcutaneous deposits of the salt.

We had the assistance of Dr. Lydia M. Gibson in administering the inorganic agents.

Table III gives the details for tuberculins and karkinolysin. The tuberculin tablets were spread in distilled water and each dose was contained in 0.3 to 0.6 millilitres. Filtrate 347 was diluted with distilled water for the smaller doses and 0.1 millilitre volumes injected. The larger doses, and the bovine tuberculin, were given undiluted. Except in two animals, all tuberculin doses were subcutaneous. Doses were given daily or at nearly uniform intervals, which appear from the tabulation.

*Controls.*—While the transplantable tumors may regress and disappear and the host die of old age or intercurrent disease, it is well known that mice bearing the spontaneous tumor almost never recover. Recovery is practically an unknown phenomenon. The tumor, however, may fluctuate in growth rate or remain stationary; and even a degree of regression is well established. According to Woglom<sup>1</sup>, about one per cent. remain stationary or regress. Complete disappearance followed by recurrence has been observed. It is not easy to identify a growth histologically and follow it to complete absorption, but the cases of regression imply the existence of spontaneous cure, however rare. We have seen none. The survival of the mice after a tumor becomes palpable varies within a wide range; three or four months is a probable average. The tumor grows slowly or rapidly and is rarely stationary. The larger tumors almost always ulcerate, the smaller ones occasionally.

TABLE III

*Tuberculin; Karkinolysin*

Tuberculin B. E. 1 mg. and .0001 mg. tablets

| Number of doses                      | Duration of treatment—days | Survival—days | Total dosage—mg. | Weight of mouse—gm. |     |       | Diameter of tumor—mm. |      |       | Remarks                           |
|--------------------------------------|----------------------------|---------------|------------------|---------------------|-----|-------|-----------------------|------|-------|-----------------------------------|
|                                      |                            |               |                  | Begin-<br>ing       | End | Death | Begin-<br>ning        | End  | Death |                                   |
| Dose: 1 milligram. Subcutaneous      |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 14                                   | 39                         | 76            | 14               | 27                  | 27  | 23    | 12.                   | 17.  | 20.5  | Surviving. Pregnant at beginning. |
| 13                                   | 36                         | 39            | 13               | 26                  | 26  | 19    | 13.                   | 16.5 | 15.   |                                   |
| 10                                   | 37                         | 130           | 10               | 24                  | 25  | 22    | 7.5                   | 7.5  | 27.5  |                                   |
| 85                                   | 87                         | 88            | 85               | 29                  | 25  | 23    | 7.                    | 17.  | 16.   |                                   |
| 98                                   | 102                        |               | 98               | 43                  | 29  |       | 6.5                   | 11.  |       |                                   |
| 9 intravenous, 4 subcutaneous, doses |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 13                                   | 13                         | 24            | 13               | 25                  | 26  | 23    | 11.5                  | 16.  | 17.5  |                                   |
| Dose: 0.0001 milligram. Subcutaneous |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 56                                   | 68                         | 92            | .0056            | 27                  | 26  | 20    | 4.5                   | 7.5  | 9.    | Max. 22.5 mm.                     |
| 56                                   | 59                         | 60            | .0056            | 25                  | 21  | 20    | 12.5                  | 21.  | 21.   |                                   |
| 66                                   | 69                         | 77            | .0069            | 28                  | 28  | 24    | 15.5                  | 26.5 | 24.5  |                                   |
| Tuberculin T. R.                     |                            |               |                  |                     |     |       |                       |      |       |                                   |
| Dose: 1 milligram. Subcutaneous      |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 17                                   | 33                         | 46            | 17               | 24                  | 27  | 24    | 7.5                   | 24.  | 26.5  |                                   |

| Dose in millilitres<br>Number of doses |     |    |    | Duration<br>of treat-<br>ment—<br>days | Survival—<br>days | Total<br>dosage—<br>ml. | Weight of mouse—gm. |  |  | Diameter of tumor—mm. |     |       | Remarks |
|--|-----|----|----|--|-------------------|-------------------------|---------------------|--|--|-----------------------|-----|-------|---------|
| .001                                   | .01 | .1 | .4 | .5                                     |                   |                         |                     |  |  | Begin-<br>ning        | End | Death |         |

Filtrate 347. Subcutaneous

|    |    |    |    |    |    |     |      |    |    |    |      |      |      |   |
|----|----|----|----|----|----|-----|------|----|----|----|------|------|------|---|
| 22 | 25 | 17 |    |    | 42 | 129 | 1.95 | 29 | 29 | 26 | 9.5  | 12.5 | 15.  | A second tumor arose.<br>Surviving. Tumor 20 mm.<br>Max. 15 mm.<br>Max. 22 mm.<br>Max. 17 mm. Second tumor arose.<br>Enormous metastases. |
|    | 25 | 17 |    |    | 42 | 67  | 1.95 | 31 | 36 |    | 9.5  | 22.  | 24.  |   |
|    | 25 | 17 |    |    | 42 | 52  | 1.95 | 25 | 24 | 24 | 6.   | 8.   | 9.5  |   |
|    | 25 | 17 |    |    | 42 | 17  | .16  | 31 | 26 | 31 | 5.   | 11.  | 19.5 |   |
|    | 10 |    |    |    | 16 | 123 | 1.7  | 32 | 31 | 19 | 15.5 |      | 14.  |   |
|    |    | 17 |    |    | 31 |     | .022 | 23 | 23 |    | 9.   | 12.  | 20.  |   |
|    |    |    | 18 |    | 22 | 27  | 7.2  | 24 | 25 | 29 | 10.  | 17.5 |      |   |
|    |    |    |    | 10 | 18 | 38  | 5.   | 30 | 34 | 30 | 8.   | 19.5 | 9.   |   |
|    |    |    |    |    | 18 |     |      | 36 | 34 |    | 8.5  | 10.  |      |   |
|    |    |    |    |    |    |     |      |    |    |    |      |      |      |   |

Intravenous

|  |    |    |  |  |    |  |      |    |    |  |    |      |  |
|--|----|----|--|--|----|--|------|----|----|--|----|------|--|
|  | 17 | 17 |  |  | 34 |  | 1.87 | 25 | 25 |  | 7. | 12.5 |  |
|--|----|----|--|--|----|--|------|----|----|--|----|------|--|

## Tuberculin B. F. (Bovine)

| Number of doses                  | Duration of treatment—days | Survival—days | Total dosage—ml. | Weight of mouse—gm. |     |       | Diameter of tumor—mm. |      |       | Remarks                           |
|----------------------------------|----------------------------|---------------|------------------|---------------------|-----|-------|-----------------------|------|-------|-----------------------------------|
|                                  |                            |               |                  | Begin-ning          | End | Death | Begin-ning            | End  | Death |                                   |
| Dose: 1 millilitre               |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 30                               | 30                         | 32            | 30               | 28                  | 23  | 21    | 14                    | 20   | 15.5  |                                   |
| Dose: .5 millilitre              |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 66                               | 68                         |               | 33               | 31                  | 32  |       | 6.5                   | 7.   |       | Max. 9 mm. Second tumor arose.    |
| Doses: 28 at 1 ml.; 57 at .5 ml. |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 85                               | 90                         | 93            | 56.5             | 29                  | 21  | 18    | 3.5                   | 7.   | 6.    | Max. 8 mm.                        |
| Karkinolysin (Hanson)            |                            |               |                  |                     |     |       |                       |      |       |                                   |
| Dose: 1 millilitre               |                            |               |                  |                     |     |       |                       |      |       |                                   |
| 15                               | 15                         | 16            | 15               | 22                  | 20  | 19    | 9.                    | 11.  | 10.5  | Rapid growth. Second tumor arose. |
| 29                               | 29                         | 30            | 29               | 31                  | 31  | 27    | 10.5                  | 26.5 | 27.   |                                   |
| 62                               | 62                         | 67            | 62               | 34                  | 31  |       | 10.                   | 19.5 | 20.   |                                   |

## THERAPY OF SPONTANEOUS MOUSE CANCER

Mice will endure enormous doses of distilled water and still more of physiological salt solution, whether intravenous or subcutaneous. Data have been published and are not repeated here. As our results are all negative, controls need no detailed consideration.

*Results.*—Since the tumor varies widely in rate of growth, it was to be expected that slowly increasing or nearly stationary growths would suggest restraint imposed by the medication. Numbers of such cases occurred. All of them have been checked by repetition until without exception every agent has been tested with a tumor whose growth was unequivocal. The tumors may be said to have run their usual course, and often to ulceration.

We are not able to find any evidence of therapy, or even definite effect—macroscopic or microscopic—on the tumor or its growth. The illusory nature of the apparent success which has sometimes followed attempts at therapy of propagated tumors is again implied. Such growths are not fit indicators of the therapeutic value of presumptive cancer treatments.

### SUMMARY

Fifty-six inorganic compounds, containing thirty-three chemical elements for which there is evidence indicating therapeutic value for transplantable cancer, have been tested for their effect on spontaneous mouse cancer.

Four forms of tuberculin and one extract of thymus have likewise been tested.

No therapeutic action was exhibited by any of these.

### BIBLIOGRAPHY

<sup>1</sup> J. Cancer Research, vol. x, p. 50, 1926; vol. xi, p. 417, 1927.

<sup>2</sup> See also, Sugiura and Benedict, J. Cancer Research, vol. xiii, p. 340, 1929.

<sup>3</sup> Abstract in Gann, March, vol. xxi, 1927.

<sup>4</sup> J. Cancer Research, vol. vii, p. 379, 1922.



# SUSCEPTIBILITY AND RESISTANCE TO TAR CANCER

AN EXPERIMENTAL STUDY

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THE clinic and the laboratory are two methods of equal value for the study of cancer. Nevertheless, certain domains of cancerology are more easily studied in a laboratory. That is why the study of tar cancer is so instructive in enabling us to follow in an easier way the early development as well as the evolution of the disease, and to study the action of a multitude of factors which could be of influence on its relation and evolution.

The object of this article is not to make an entire study of the matter—not even a bibliographic study of the problem. What we desire is to give an account of our experiences in studying the part played by the organisms as a whole in the etiology of tar cancer. In the latter one, as in any other cancer, there are in reality determining local factors and a general organic resistance. Certain authors believe that the local factors, called the irritating factors, are of physico-chemical order; others are inclined to think that they are of infectious nature, infection the bed of which has been prepared through local irritation. The general organic receptivity concerning tar cancer is no longer debatable. The point is now to determine the importance of the organic receptivity for the germination of the cancer and to establish, if possible, the nature of this receptivity. Concerning particularly the tar cancer, we should like to show how far we have come in this study.

*Demonstration of the Existence of a Predisposition to Tar Cancer.*—It will be remembered that the first scientist who proved the existence of a species, racial, individual and even a singular predisposition (receptivity) against experimental spiroptera-cancer, is Fibiger. His experiments are models of classic studies for cancerologists.

Lipshutz, and later, in 1922, Roussy, during the first gathering of the “Leewenhock Vereeniging” drew attention to the fact that all the mice submitted to the same tarring did not produce cancer equally. Some animals seem to be quasi refractory to it.

Later, Bang and Leitch have shown that a tar-cancer sprang up in a mouse several months after the cessation of the tarring (the quasi specific irritation of Teutschlaender). The final outbreak of the cancer process has thus nothing to do with the actual presence of the tar itself. The tar is necessary as a quasi specific irritating factor for the preparation of the soil, but after this is done the process goes on without it. One could say that it has put into motion a mechanism the end-result of which is the cancer. This being so, we have asked ourselves if this fatal and slow work of cancerization of the cell is influenced by the metabolism of the individual.

Since 1923, we have shown that the tarring is modifying the organic medium to such a degree that this alteration contributes to the development of cancer. In fact, if we painted the necks of a series of animals during a short period (two months, for instance) only a few animals would develop cancer—approximately 20 per cent. But if we continue the paintings on another region, at a certain distance from the former one, for two months more, we see that a much greater number of animals (71 per cent.) produce cancer on the first area painted. With Masse, I have shown afterwards that by injecting tar in small amounts under the skin of the abdomen of a series of mice during three to four months, carefully avoiding soiling the skin surrounding the injected point, we prepare the animal organism to produce cancer of the skin at a distance far from the injected spot: If we paint the injected animals on the neck during two months we produce a large percentage of cancer (58 per cent.) while the controls (painted the same time but not injected) present only 15 per cent. of cancer. Another series of controls, painted at the same time during a period of two and one-half months, gave only 30 per cent. of malignant growths. Moreover, several cases of “spontaneous” mammary cancer developed among the injected animals not bearing skin cancer and the skin cancers develop earlier and are more malignant than those of the control animals (50 per cent. of metastasis among the injected, 20 per cent. among the controls).

Merteus, in the same order of ideas, established that the papillomas and the “histological cancers” of the ear of a rabbit regress if one stops the tarring of the diseased ear, but the same kind of tumors continue their growth if one paints the other ear.

Since that time our researches have been confirmed by Beck, Fischer-Waesel, Soboleva, Schwabad and Schov, Kreyberg, and some others. Kreyberg was able to produce cancer with metastasis in animals poisoned with tar only by burning their skin. Lynch, in the laboratory of Murphy, has increased in a considerable proportion the percentage of spontaneous tumors of the lungs in a susceptible strain of mice painted various times with tar, a very short period on each spot, in order to avoid the apparition of skin cancer. The tumor age of those animals was also markedly lowered.

So it appears duly established that the alteration of the animal metabolism as the result of chronic intoxication by tar, contributes to the elaboration of cancer on chronically irritated spots.

*The Rôle of Certain Metals in the Predisposition to Tar Cancer.*—It would be impossible to study here the action of all the metals which have been tried in various laboratories. We shall speak only of those which have been particularly studied in this institute.

One of our pupils, P. Estas, has, at our request, been studying the action of copper and has established the fact that when used in feeble doses it has a retarding effect on the development of tar cancer as well as on

its evolution. When used in strong doses, the metal, which is very toxic, has quite the opposite action.

Sensational affirmations having been spread about, we have asked Estas to study the action of magnesium. We used magnesium sulphate in injections, the animal of experiment being the mouse, as it is the only kind that easily makes tar cancer of a real malignant character (physiological cancer, following our terminology). The details of these researches are consigned in Estas' thesis; we state here only the conclusions of it: Magnesium given in suitable doses is capable of delaying the apparition and the evolution of the tar cancer in the mouse. To obtain a real effect one must give at least one centigram a week to a mouse. Delbet believes that magnesium chloride is more effective. Honoré, one of our pupils, was able with this salt to confirm Estas' results.

Consequently, it seems established that certain metals when introduced in suitable doses in the metabolism of diseased individuals are capable of influencing the development and evolution of tar cancer by retarding them.

We have asked ourselves also whether certain other metals should not have quite an opposite action.

It is well known that certain authors attribute to arsenic a rôle in the evolution of cancer (accelerating action). In the different experiments we have tried to elucidate this rôle but have not succeeded, so that we cannot have a personal opinion on the matter. *Per contra* we have studied the action of different radioactive substances, especially the action of ionium and the action of a composed salt of thorium-uranium. We have chosen those substances out of the radioactive series because they have practically a constant and weak radiancy and also because they issue only particles. So we have to pay attention only to a sole type of radiation quasi entirely absorbed by the cells where the radioactive ion has its abode. We may also inject relatively considerable doses without provoking an aplastic anæmia. When we inject those metals intravenously, they settle first in the reticulo-endothelial system. On account of the great energy of the particles one can suppose that they have an influence on the metabolism of the system. Those particles form an energetic power of synthesis for the hydrocarbons (Mund) and they are able to transform ergosterol into the antirachitic vitamine D (Maisin, Pourbaix, Mund, Castille).

At any rate, the animals which have had strong doses of ionium before the tarring and those which have had only a small quantity during the paintings produce cancer more easily than the animals of control which have not been treated by ionium and their cancers are more malignant.<sup>2</sup> The results are as follows:

We have shown with Ledecq and Estas that ionium has the same effect on rabbits. Since the experiences of Tamagiwa and Itchikawa, and especially since the work of Leroux, we know that tar cancer in rabbits is seldom progressive. It regresses and disappears easily after the cessation of the tar painting. It is those cancers we have called "histologic can-

# TAR CANCER

*Absolute Percentage of Cancer*

| Number of days         | Injected<br>per cent. | Controls<br>per cent. |
|------------------------|-----------------------|-----------------------|
| 150.....               | 40.6                  | 18.7                  |
| 210.....               | 78.1                  | 56                    |
| End of experiment..... | 87.5                  | 72.9                  |

N.B.—We call “absolute percentage of cancer” the percentage of animals producing cancer among those which have lived after the appearance of the first cancer in the series of animals.

cancers” in opposition to progressive and metastasizing cancers which we have called “physiologic cancers.” A great number of our rabbits injected with ionium produce “physiologic cancer” (more than 30 per cent.) while their controls painted during the same length of time never produce a progressive cancer but only “histologic cancers.”

We have obtained similar results with injections of ionium in fowl (production of large embryoma in injected chicken, and even malignant tumors—Maisin and Dupuis).

In 1929, Spies and Picard studied in our institute the effect of Hocking’s fluid (a composed colloidal salt of uranium-thorium) on a grafted mouse tumor. They found that this compound accelerates the tumor growth.

We believe that the action of some metals on the development and evolution of tar cancer is quite an established fact. Certain metals have a retarding action, others, an accelerating effect. The mechanism of those actions is not yet understood and can be elucidated only by experiment. At the end of this work we shall discuss the matter.

*The Rôle of Certain Physiologic Functions in the Predisposition to Cancer.*—It is absolutely necessary before speaking of some of these functions in particular to consider the question briefly in a general way.

In fact, one can conceive the action of certain physiologic functions on the cancer from two different points of view. Some of these functions could have an effect on the local determinism of a tumor. For instance, disturbance of the lactation, as Bagg showed it, could provoke congestion and chronic inflammation in the mammary gland of the mouse and cause the apparition of a breast cancer in susceptible animals. Various stasis of organic fluids could, as it appears, lead to the same result. Considering this from the physiologic point of view, concerning the interaction existing between certain glands with internal secretion, one must remember the interesting communication of Goormagtig showing that repeated injections of folliculin are capable of producing adenoma of the breast in mice. On the other hand, it is impossible to deny the action of the ovaries on the development of uterine fibroma. It seems probable that other similar facts will be proved in the future for other tumors.

At any rate, these influences are acting as local determining factors on the development of a tumor in a predisposed individual at any given spot. Considering another point of view one could ask whether certain organic

functions, as, for instance, the metabolism of fats or of the nucleoproteids, are injured in animals predisposed to cancer and whether those lesions should not be one of the important factors in cancer predisposition.

It is from this point of view that we have been studying the testicular function of mice in its connection with cancer and recently the function of the thymus and also the metabolism of fats.

In 1925, we pointed out with Desmedt and Jacqmin the particularly rapid evolution of tar cancer of a group of castrated mice which had given a considerable percentage of metastasis. I have asked Jacqmin to continue the study of that question. In his thesis he confirms these first observations. A point quite established during the researches of Jacqmin is one showing that mice castrated before puberty are not at all refractory to tar cancer as they are refractory to implantation of transplanted tumors (Strong, Murphy). One could even assert that those mice are more susceptible than normal mice of the same age and strain, tarred at the same time; the percentage of cancer and of lung metastasis is higher than in the control group.

For several years one has considered the thymus played a rôle in the genesis and evolution of cancer. Fichera was one of the first to study this question. Recently, Babes, while studying the effect of tar intoxication on rabbits, has noticed a very rapid and marked destruction of the thymus in tarred animals. In the United States, Hanson has been trying the action of certain thymic extracts on human cancer and he relates four cases where he seems to have obtained encouraging results.

In our Institute we have asked Miss François to study that question. She noticed that tarred mice, fed with thymus diet and refractory to cancer, had, in spite of their age, persistence of remnants of thymus abnormality well conserved, thymus which has almost entirely disappeared in normal animals of the same age and which is non-existent in animals that are bearers of tar cancer. These observations, added to the results obtained by other workers, deserve the attention of cancerologists and suggest new researches in this domain.

We have not had the opportunity of studying personally the action of the suprarenal, the ovaries, the thyroid, the hypophysis and pineal gland on experimentally induced cancer, but several publications have appeared concerning those questions. Nevertheless, I am obliged to mention especially the work of Loeb, pointing out the influence of the ovariectomy before puberty on the development of spontaneous breast cancer in mice as well as the recent work of G. Coffey and J. Humber, Arloing and Sokoloff on the influence of suprarenal gland on transplanted tumors and on human cancer.

*Influence of Diet on Tar Cancer.*—Since the remarkable work of Minot and his assistants showing the influence of liver diet on pernicious anæmia, we have tried the action of various diets on tar cancer. As it is already established with certain evidence that general susceptibility plays an important rôle in the development of cancer, one has a right to think of the diet in trying to modify this susceptibility. In fact, the discovery of Minot, and those

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concerning the different vitamins show how certain food factors have an influence on various affections, which one never thought could be influenced by diet.

(A)—*Influence of the Liver Diet on Tar Cancer*.—In 1928, we published with Miss François our results concerning the action of the liver on the genesis and the evolution of tar cancer. We showed that mice submitted to this diet produce the cancer more quickly and in a higher percentage than the animals of control. These cancers are very malignant and produce a high percentage of lung metastasis. Since that time, Miss François, continuing the study of this question, has several times repeated the same experiment. If one makes the total out of the number of animals that have been living long enough to produce cancer, one reaches the figure of 113 for animals nourished with liver and the figure of 132 for the animals of control which had another diet—either vegetarian or a mixed one of meat and wheat. Being grounded in those important figures, she was able to state that the liver diet activates the genesis of tar cancer and its evolution. These are the principal results of her experiments:

*Absolute Percentage of Cancer*

| Number of days since beginning of experiment | Liver diet per cent. | Controls per cent. |
|--|----------------------|--------------------|
| 120.....                                     | 10                   | 4                  |
| 150.....                                     | 46                   | 17                 |
| 180.....                                     | 69                   | 39                 |
| 210.....                                     | 76                   | 59                 |

*Percentage of Lung Metastasis*

|               |      |
|---------------|------|
| Liver.....    | 49.3 |
| Controls..... | 29.3 |

Note.—A certain number of animals being still alive, the percentage of metastasis could still vary, but only within small limits.

The liver diet has the same influence on the tar cancer of rabbits and on the "histological cancer" of the gall-bladder of the guinea pig (Ledecq).

Pushing these researches further, we have succeeded in showing that the active substances resist desiccation and are still contained in the liver powder thoroughly washed with ether in order to extract the fats. Those hepatic fats are quite inactive; perhaps their action is an inhibiting one, but more data is necessary to prove it. The liver extract of the "Nordman Werk" of Hamburg, which is rather active for pernicious anæmia, has a slightly activating effect, but surely less marked than that of liver or liver powder. The extract No. 343 of Eli Lilly (Minot), which is very powerful against pernicious anæmia, is deprived till the 160th day at least, of any activating influence on the development of cancer. The following is the result of this experiment:

*On the 180th Day Since Experiment Began*

|                                 | Cancer | Papilloma | Free of lesions |
|---------------------------------|--------|-----------|-----------------|
| Liver diet . . . . .            | 10     | 4         | 0               |
| Raw-beef diet (muscles) . . . . | 5      | 8         | 1               |
| Lilly extract 343 . . . . .     | 4      | 6         | 5               |

Of all these researches we can conclude that the liver contains stimulating substances. They are resistant to desiccation and not included in hepatic fats. They are not to be identified with the anti-anæmic substance of Minot.

(B)—*Influence of Different Other Diets on Tar Cancer.*—We have already mentioned that hepatic fats seem to have possibly an inhibiting action when compared with a raw-beef-muscle diet or a purely vegetarian one. A brain diet, rich in lipoids, too, seems to have the same action, but more marked. This new statement corresponds to the researches of Sugura and Benedict, who showed that brain diet has an inhibiting action on the growth of a transplantable rat tumor. Our results are based on a smaller number of animals, and for this reason we wish to repeat the experiment before we affirm the above-mentioned results.

Animals nourished on a diet composed of a mixture of flour and raw-beef muscle (forty animals) show a small acceleration in comparison with animals nourished on flour alone or on a diet composed of flour and hepatic fats or flour and brain.

Animals fed with a mixed diet, flour and intestinal mucosa, or a diet of flour and splenic extract of the "Nordman Werk," have not shown any characteristic evolution.

*Per contra* we should like to insist upon animals fed on a mixed diet, flour and thymus three times a week. By means of this diet we have made two experiments, each one with about fifteen to twenty animals kept alive after first appearance of cancer and controlled by a group of animals fed with a mixed diet of flour and raw-beef muscle. The first experiment has shown a considerable retardment in the development of cancer; the second has given the same result in a less marked degree. If one takes the figures of the two experiments and compares them to the figures of the two control experiments with flour and muscle diet, one notices a real retardation in the development of cancer among the thymus-diet mice.

An extremely curious fact to be noticed is the growth of the cancer of the thymus-diet animals after its beginning. Those cancers grow very well, giving big tumors with a high percentage of metastasis. The action of thymus diet seems to be only a preventive and not a curative one. We are repeating these researches in order to collect more data. I have already mentioned that animals fed with thymus were of remarkable health and that mortality was very low in the course of the tar paintings. Often, two months after tarring, animals which have no tumors show a growing up of hairs on

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*Absolute Percentage of Cancer*

|              | 150 days<br>per cent. | 180 days<br>per cent. | 240 days<br>per cent. |
|--------------|-----------------------|-----------------------|-----------------------|
| Thymus.....  | 9                     | 18                    | 44                    |
| Muscles..... | 19                    | 35                    | 55                    |
| Liver.....   | 46                    | 69                    | 81                    |

the level of the tarred spot and their coat is so beautiful that one could believe them to be fresh animals.

(C)—*Tar Cancer and Vitamine A*.—On account of the researches of Burrows, Gasparri, Taiki, Rhoda Erdman and others on the action of vitamine A on the development of spontaneous cancer, on the transplanted mouse cancer and on the growth of cells *in vitro*, we have asked Trigaux to study the effect of this vitamine on tar cancer. We have studied its action by feeding and by injection. We have used the product Y of the Lever Brothers and Company, which contains no vitamine D and is very rich in vitamine A. The mice were fed with a mixed diet—raw muscle and flour. A group of these mice, in addition to the diet, received vitamine A three times a week, at a dose which was the limit of toxicity of the Y product for mice. A second group received the same amount of vitamine subcutaneously. The control animals were fed with the same diet without vitamine A and a certain number of them were given, three times a week, an injection of olive oil in the same amount as the product Y injected in the animals of experiment.

Our present results show that vitamine A introduced as a supplement in the normal alimentation of mice has no retarding effect on the development of tar cancer. On the contrary, this group is in advance when compared with the controls. As for the injected vitamines, we cannot affirm anything with certitude because the mortality was very high and the number of animals which survived the appearance of the first cancer was not a very important one.

### GENERAL DISCUSSION

Many years ago it was proven that some hormones have an influence on the growth of tissue. Lately one has shown the influence of vitamine A on the growth. Since the discovery of Minot one knows the action of certain substances contained in the liver on the formation of the red corpuscles of the blood. Recently, Castle seems to have proven that the active substances of the liver are products of a normal digestion of meat in the stomach, products which are stored up in great abundance in the liver.

These substances are consequently of quite a different order from those of vitamine A or C which seem not to be able to form themselves regularly in our organism. They have a certain analogy of origin with vitamine D which can also be formed in our organism under the influence of ultra-violet rays. But, anyhow, it is the first time one suspects that normal products of a normal digestion have an influence comparable to a hormonal influence—



action at a distance on a well-determined function. The growth of different tissues is, therefore, dependent on definite chemical substances secreted by certain glands (hormones) or absorbed (vitamines) or even produced by normal organic functions (digestion).

Certain benign tumors are in connection with organic dysfunctions. Has the cancer, a malignant tumor, infectious or not, any relation with one definite or certain well-known organic function?

We showed at the beginning of this work that the general intoxication of the organism by the tar is playing an obvious rôle in the genesis of the carcinomatous process. Pushing our investigations forward, we wish to show by means of what mechanism this intoxication is acting. We have seen that certain alimentary substances contained in the liver facilitate the apparition of tar cancer; others, like magnesium, certain fats or possibly certain albumins (nucleoproteids) have a retarding effect. On the other hand, injection of radioactive metals activates the apparition of the same tumors. These metals have their abode in different organs but especially the reticulo-endothelial system. Possibly their action is the result of an alteration of a certain function, for one finds less injected substance in the tumor than on the level of most of the internal organs and also because they exert their action on the organism before the apparition of the tumor in order to favor its development.

In that way the action of metabolism on the genesis of tar cancer can in one way be influenced by ingestion of certain substances; in the other way, by alteration of certain functions (radioactive metals, castration, *etc.*). Henceforth, one is asking oneself whether the predisposition to cancer is not the result of the presence of certain substances in more or less abundance in our organism, activating substances on one hand, and inhibiting on the other. These substances can be absorbed, be the result of a sort of alimentary intoxication or proceed from a defective organic metabolism. In the first case, predisposition and resistance might be only transitory while in the second case the predisposition would be a permanent phenomenon.

One could try to examine the problem still nearer by producing other experiments of the same order as those which have been the topic of this article; or else try to solve the question by investigating the chemical modifications which take place in the blood during the production of cancer. In this way, one would still have to establish the relation from cause to effect between those modifications and the cancer.

We have asked Miss Pourbaix, chemist of our institution, to study the variations of the serum of rabbits injected with ionium and those of rabbits painted with tar. She has been following the variations of different groups of substances but has concentrated her efforts especially on the variations of cholesterol, a substance often considered as playing a rôle in the evolution of cancer. She has come to the conclusion that a little before the appearance of tumor and during the evolution of the cancer, cholesterinæmia is very unstable, the variations often being quite marked. It seems that

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animals intoxicated and prepared to produce cancer or bearing cancer show great disturbance of the metabolism of fats and are incapable of maintaining their lipæmia in normal conditions.

All these researches force us to admit that the metabolism is playing an important rôle in the genesis of cancer and incite us to investigate in which way the metabolism is lacking.

### CONCLUSIONS

1. Tar cancer is the result of a local irritation as well as of a general intoxication of the organism.

2. Certain mineral salts used in convenient doses are capable of delaying the appearance of cancer (magnesium, copper) and of lowering the percentage of induced tumors.

3. Other salts, for instance, salts of radioactive metals, have quite an opposite effect.

4. Diet can influence the appearance and evolution of tar cancer.

5. The liver diet activates the development of tar cancer.

6. It is probable that other diets would retard its appearance.

7. Vitamine A absorbed in addition to a normal alimentation has no inhibitive effect on the appearance of cancer.

8. Preceding closely the development of tar cancer and during its evolution, the metabolism of fats is deficient and the variations of the cholesterinæmia are marked. The same variations are to be noticed after repeated ionium injections.

# EXPERIMENTAL AND CLINICAL STUDIES ON THE TREATMENT OF CANCER BY DICHLORETHYLSULPHIDE (MUSTARD GAS)

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THE experimental and clinical investigation reported herein was suggested to the authors by Dr. James Ewing who while serving at the United States Army Medical Museum during the late war, was impressed by the peculiar and specific nature of mustard-gas burns. There are certain characteristics of the mustard-gas reaction which suggest the use of this chemical in the treatment of neoplastic growths.

The action of mustard gas ( $\text{CH}_2\text{ClCH}_2$ )<sub>2</sub>S on normal tissues is well known. Since its introduction in 1917 as an agent of chemical warfare much has been written concerning its pathological effects. Warthin and Weller, in 1919, and the report of the Medical Department of the United States Army, in 1926, give a summary of the more important clinical and experimental studies. The action of mustard gas on human tissues has been extensively studied by many observers. The names of Guthrie, Victor Meyer, Winternitz and Underhill are but a few of the well-known workers in this field. An excellent chapter on the subject of "Burns by War Gases" may be found in the recently published book, "Burns," by Pack and Davis.

A mustard-gas burn is very unlike that produced by heat or the corrosive acids. It differs from the heat burn in that there is no thrombosis of vessels; a more intense amount of œdema occurs; the effect is progressive even at times continuing for five to ten days. The zone of necrosis gradually increases for a period, at which time an equilibrium is reached and repair sets in. The blood-vessels are collapsed and tremendously damaged. Intense leucocytosis occurs.

The more severe effects of mustard gas on human skin are characterized by intense hyperæmia; œdema; the formation of vesicles and sometimes pustules of the surrounding tissues; finally, ulceration of the epidermis. This process is essentially local in its action, is accompanied by a pronounced leucocytic infiltration and is characterized by the relatively long duration of action.

It is our experience that immediately following the application of a drop of the mustard-gas solution to a cancer of the skin there is a temporary blanching of the lesion and surrounding epidermis. If the lesion is covered with epithelium there will be practically no pain resulting from the application; otherwise a burning sensation results. Within two hours following the application of the solution, the blanching and anæmia are followed by a hyperæmia. Within forty-eight hours, œdema and vesiculation are well established. This phase is followed by the processes of beginning repair.

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For the purposes of carcinoma therapy, we disregard the differences of absorptive properties of the skin in different patients.

In 1927 Doctor Ewing suggested to one of us (Bagg) the study of the effect of mustard gas on experimental cancer in the lower animals. This in turn led to the application of this chemical to certain localities, such as the mouth, bladder and rectum of normal animals, as well as a study of the effect of varying the dosage of the solution upon normal skin.

It is the purpose of this paper to summarize the results of our studies of the effect of mustard gas on normal and neoplastic tissues in the lower animals and to record the history of twelve cancer patients treated by this chemical at the Memorial Hospital.

*Methods.*—The concentrated mustard gas was obtained from the Depart-



FIG. 1.—The illustration shows the reflected skin of a rabbit. The abscess at the top of the photograph has been cut open and one wall reflected. Upper lesion treated with one minim of mustard gas on surface of the skin. Lesion in the middle resulted from one-half minim and the lower lesion from one-quarter minim. For further details, see text.



FIG. 2.—A mustard-gas eschar is shown with the remnant of a tar cancer in its centre. Animal killed twenty-six days after treatment.

ment of Chemical Warfare Service of the United States Army. Great care was used in handling the solution. The concentrated liquid was kept in a chemical hood and exposed to the air only when the exhaust fan was in operation. The mustard gas was dissolved in absolute alcohol. A small quantity (usually 2 cubic centimetres) was made fresh for each experiment and kept in glass-stoppered bottles. A calibrated glass pipette was used in applying the solution to the surface of tissues. This pipette delivered drops of approximately  $\frac{1}{4}$  minim each and this amount was the standard dose used in both the clinical and experimental treatments. Treatments of small animals were made inside the laboratory hood, which carried the fumes away from the operator. We have found that it is well to have all treat-

ments to the larger animals or humans done near a hood, or in a situation where very adequate provision is made for prompt withdrawal of the fumes of the mustard gas. After the treatment, the glass pipette or the syringe was thoroughly rinsed in concentrated nitric acid, which stops the action of the mustard gas. When the mustard gas is applied to the surface of a tumor the absolute alcohol acts as a vehicle, evaporating almost immediately, leaving the mustard gas as a thin film on the treated surface. When relatively small skin cancers were treated, a ring of vaseline was placed near the margin of the tumor to check the spread of the solution too far beyond the limits of the growth.

*Experimental Results—Mustard Gas on Tar Carcinoma in Mice.*—The scope of this paper does not permit a detailed account of the animal experimentation. A more com-



FIG. 3.—Microphotograph of a section through an untreated tar cancer in the mouse.



FIG. 4.—Microphotograph of a section through the centre of the lesion shown in Fig. 2. There is apparently complete destruction of the tumor. (Dose, one-quarter minim mustard gas.)

plete report of this phase of the work will be given at a later date. There are certain general deductions which may be drawn from these studies that are of clinical interest and therefore will be mentioned briefly.

It was found that when mustard-gas solution (20 per cent. in absolute alcohol,  $\frac{1}{4}$  minim drop) was applied to the skin of the back of an adult mouse there was a severe toxic reaction. The treated skin became tough, thickened and dry. There was pronounced œdema of the subcutaneous tissues and adjacent muscles and the animals died from one to four days later respectively.

When a similar dose of mustard gas was applied to the back of a mouse on which a tar cancer had been previously produced, the presence of the neoplasm itself and possibly the conditions produced in the adjacent skin as a result of long tarring, appeared to protect the animal from the severe general toxic reactions noted when mustard gas was placed on normal skin. Such a reaction was noted in an animal that showed a small

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papillary growth in the tarred area of the back after seventeen weeks of tarring. At the twenty-seventh week there were three tumors, raised about two millimetres above the skin and covering an area 9 by 15 millimetres. The growth was treated with  $\frac{1}{4}$  minim of 20 per cent. mustard gas in absolute alcohol. A heavy eschar appeared which involved the tumor area and adjacent skin. The scab was lost ten weeks later, the skin beneath was apparently normal and there was no local return of the growth. The animal died approximately eleven months after the treatment. Autopsy revealed a metastatic nodule in one lung.

*Mustard Gas on Normal Tissues.*—In order to test the effect of varying the dosage of mustard gas in relation to the degree of tissue reaction, six skin areas of the back of a large rabbit were treated with varying amounts of a 10 per cent. mustard-gas solution in absolute alcohol. A glass pipette delivering drops of approximately  $\frac{1}{4}$  minim was used. The animal was killed two weeks after the treatment, the skin was reflected and the following record shows the dimensions of the resulting lesions:

Area 1: Dosage,  $\frac{1}{4}$  minim mustard gas solution; lesion 20 by 20 millimetres.

Area 2: Dosage,  $\frac{1}{2}$  minim mustard gas solution; lesion 32 by 30 millimetres.

Area 3: Dosage,  $\frac{3}{4}$  minim mustard gas solution; lesion 45 by 28 millimetres.

Area 4: Dosage, 1 minim mustard gas solution; lesion 50 by 50 millimetres.

Area 5: Dosage,  $\frac{1}{2}$  minim mustard gas solution; lesion 35 by 28 millimetres.

Area 6: Dosage,  $\frac{1}{4}$  minim mustard gas solution; lesion 23 by 16 millimetres.

Fig. 1 shows the reflected skin of the right side of the body and the lesions resulting from  $\frac{1}{4}$ ,  $\frac{1}{2}$  and 1 minim doses respectively. The abscess resulting from the larger dose is shown at the top of the illustration. The median wall was cut and reflected to one side. The smaller lesions, as shown in the illustration, were well localized and limited by the fascia of the underlying muscles. The lesion resulting from the 1 minim dose was also largely limited by fascia, but at one point the underlying muscles were superficially involved as well. The animal was killed two weeks after treatment. The lungs, kidneys, liver and other viscera were examined and found apparently normal.

*Clinical Experimentation.*—The agent was applied to thirteen patients, most of whom were suffering with cancer in one form or other. Brief reports of these cases appear below. They include cases of squamous carcinoma of the skin, melanoma, neurogenic sarcoma, epithelioma of the penis, *etc.* Twelve of the patients were treated by applying the solution of mustard gas to the external lesion. One patient, a remarkable case, was treated by injecting this solution intratumorally; a terrific reaction resulted but a neurogenic sarcoma several times recurrent has practically disappeared following this violent therapeutic reaction. So that we feel the possibilities of using this agent therapeutically lie not only in external application but also in interstitial doses. In fact, the latter method to date is more impressive.

We fully recognize that this agent has been applied in our cases too recently for us to report cancer cures. But as it takes so many years to report cures we are hoping that such a preliminary report may suggest possibilities to other investigators.

CASE I.—*Epithelioma.*—Male, F. R., aged thirty-one, a government clerk, seventeen years previously was treated with "Fowler's solution" for nervousness. He took 30 drops per day for a period of six months. In May, 1929, he noted a small lump the size of a pea just to the right of the anus. It increased in size and ulcerated. The lesion was

excised at Walter Reed Hospital, Washington, D. C. Pathological report, "squamous carcinoma." Wound did not heal so the patient went to the Mayo Clinic where a wider excision was made September 25, 1929. The wound was sutured and healed *per primam*. About August, 1929, there appeared numerous cutaneous nodules over the body, arms, and legs. The lesions were small, flat, encrusted and gradually enlarged. November 8, 1929, one on the right chest wall was excised at the Naval Hospital. The microscopic report was "squamous-cell epithelioma." In November, 1929, a skin specialist excised a small lesion from the right arm which microscopically was also reported to be epithelioma.

On physical examination, besides the scars of previous operations, numerous skin lesions were found all over the integument. The lesions varied from 0.5 to 1.5 centimetres in diameter. The edges were raised, crusted and grayish in appearance. These lesions included both hands. On December 6, 1929, a drop of mustard-gas solution was applied to a lesion on the chest wall, 1.5 millimetres thick and 1 centimetre in diameter; also

to another smaller lesion on the forearm. These lesions reacted typically to the application of mustard gas. (See Fig. 6.) These lesions disappeared and were replaced by thin derma. Fig. 7 shows these lesions forty-four days after the application of the solution. There has been no recurrence. The scars are pliable, well healed and painless.

#### CASE II.—*Epithelioma*.—

A. H. F., male, aged fifty, came to the Memorial Hospital November 30, 1929. About fifteen years earlier his physician had given him 5 drops a day of "Fowler's solution" over a long period. At this time he noted small red spots over the dorsum of both hands. Similar lesions later appeared over his body. In 1917 he had developed le-



FIG. 5.—This shows a mustard-gas lesion of the tongue of an adult rabbit that had been treated with a surface application of one-quarter minim of mustard gas. Animal killed three days later.

sions over the back, abdomen, chest, hips and hands. While in France, he was seen by Darier who advised radium. Placques were applied over five lesions and they cleared up. Many more lesions developed generally over the body. No treatment seemed to improve them.

In 1925 an ulcerated lesion the size of a half dollar developed on the dorsum of the right hand. This was excised by Doctor Neal, of the Howard Kelly Hospital in Baltimore, who later skin-grafted the area. Pathological report of the tissue was "epithelioma." In 1927 an ulcerated area on the right foot was excised. In 1928 an ulcerated lesion over the right hypothenar eminence was removed. A skin graft was made but failed to take. It steadily extended. Radium placques were applied to the lesion with no avail. Biopsy taken in October 1929, at the Walter Reed Hospital was reported "squamous cancer."

The patient had developed a large ulcerating lesion also on the dorsum of the left hand. On coming to the Memorial Hospital the lesions were numerous and widely scattered as indicated in Fig. 8. The right hand was amputated as it had ulcerated to the tendons and bone. Several lesions over the body and behind the left ear were treated

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Fig. 6.—Showing the lesions of the chest-wall and forearm three days after the application of the mustard-gas solution. The lesion and surrounding tissues are covered with vesicles (Case I.)

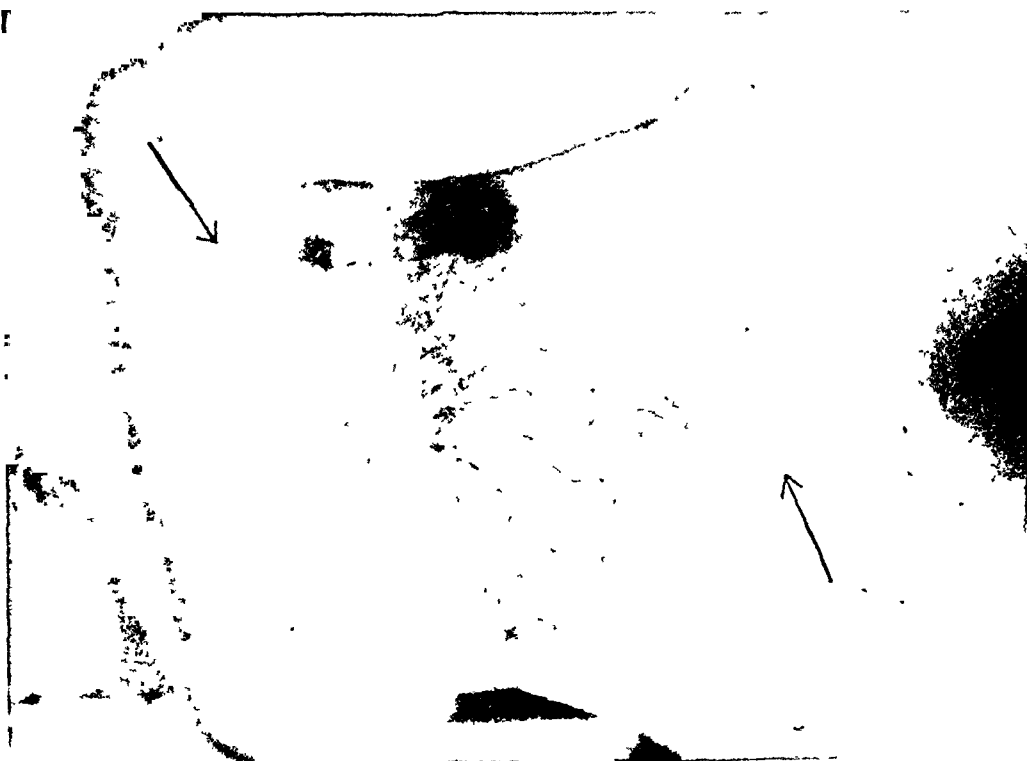


Fig. 7.—Showing the appearance eleven days after that of Fig. 6. The lesion is in the repair stage. (Case I.)



by applying  $\frac{1}{4}$  minim of the mustard-gas solution. It was necessary in some instances to give more than one application to destroy the lesion completely. Fig. 9 shows a widespread lesion behind the left ear. Fig. 10 shows this lesion during the process of destruction. Today, six months after the original treatment, the lesion is entirely gone. This is true also of those lesions which were treated by this method over the body and back. The scars are soft and to date there is no recurrence where this was applied.

CASE III.—*Recurrent Neurogenic Sarcoma.*—*The Interstitial Injection of Mustard-Gas Solution.*—H. J., male, aged forty-eight years, came to the Memorial Hospital

December 3, 1929, suffering from a recurrent neurogenic sarcoma of the right thigh. During the past five years, the patient has been operated on four times unsuccessfully for a mass lying beneath the skin of the anteromesial aspect of the thigh. Chest plate is negative for metastasis to lungs. No inguinal nodes palpable. Into the recurrent mass 3 centimetres in diameter lying over the saphenous vein, 3 minims of the mustard-gas solution were injected intratumorally on March 3, 1930. One week later for a distance of 20 centimetres from the site of injection on all sides, there was intense skin redness, board-like induration, heat and tenderness. This subsided gradually, leaving an opening which drained sero-sanguineous discharge. Portions of the tumor were occasionally extruded through the small slough of skin. October 13, 1930 (eight months later), there is a thin disk-like lesion remaining which



FIG. 8—Showing the wide distribution of the epitheliomata and keratoses (Case II)

in all probability is a completely devitalized tumor, now replaced by fibrous tissue.

The reaction was of a most intense nature, precluding the use of more than 3 drops at one time.

CASE IV.—*Melanoma.*—R. W., male, aged thirty-five, came to Memorial Hospital October 15, 1929, having a large, fungating, foul-smelling melanoma of the plantar surface of the right foot. The disease had spread widely in the subcutaneous tissue of the leg and thigh. There were also many confluent nodes in the right inguinal region. It was a hopeless case as the extent of the disease precluded an amputation of the thigh. The large foot lesion drained serum which kept dripping continuously. In an effort to reduce the size of the lesion and to prevent such loss of body fluid, applications of mustard-gas solution were made. The lesion was cauterized by these applications. There was a marked shrinking in size, a crust formed over the lesion and there was comparatively

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little loss of fluids. The patient later died of metastatic disease into the spine causing complete paralysis below the waistline.

The application in this case was of real value—reducing the size of the lesion, the odor of the lesion and the loss of body fluids.

CASE V.—*Melanoma*.—J. J., male, aged sixty-two, came to the Memorial Hospital January 25, 1930. On the abdominal wall, situated below and to the right of the umbilicus, is an elevated, mushroom-like tumor which is smooth, measures 2 centimetres in diameter, and is pigmented black. No regional nodes or masses palpable. A diagnosis of melanoma was made.

The lesion was treated January 28, 1930, with 8 drops of mustard-gas solution applied to the surface—4 drops were placed at the base, sides and covering the entire tumor. January 30, 1930, 4 drops were placed on the surface of the tumor. February 4, 1930, the tumor was smaller and more shriveled in appearance. Five drops of mustard-gas solution were applied to the tumor. February 6, 1930, the tumor has reduced a half in size. February 12, 1930, the tumor was widely excised going down to the anterior sheath of the rectus muscle and removing a wide area of skin and subcutaneous tissue.

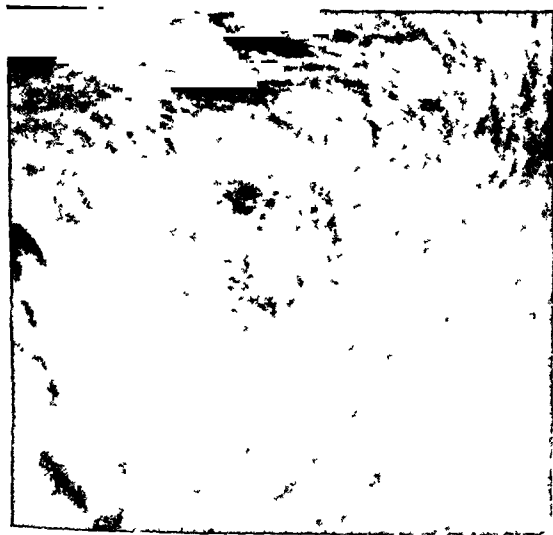


FIG 9—Showing the lesion of the scalp before the application of the mustard gas solution



FIG 10—Showing the lesion during the repair process.

*Microscopic Examination*.—Melanoma, much destruction of tumor and surrounding skin and subcutaneous tissue.

October 13, 1930, no evidence of recurrence. This case illustrates that repeated applications of this agent are possible, and that practically total destruction resulted from three applications.

CASE VI.—*Neuro-fibroma*.—H. G., female, aged forty-eight, came to the Memorial Hospital September 8, 1929, to receive treatment to three lesions. One was a red, indurated lesion situated in the left upper arm, apparently attached to the subcutaneous tissues. Another was located below the angle of the right scapula but more protruding and superficial. On the left heel was a projecting lesion having the appearance of a wart. The first lesion was treated by Doctor Craver with 200 millicurie minutes of the radium bulb, the second lesion had 71 millicurie minutes applied. To the third, on the heel, was applied 200 millicurie minutes. The lesions of the arm and back remained unchanged. The heel lesion disappeared.

The arm lesion was excised and proved by microscopic examination to be "chronic inflammatory tissue with slight productive fibrosis of subcutaneous tissues." On January 23, 1930, to the lesion on the back was applied  $\frac{1}{4}$  minim of mustard-gas solution. This was followed by the customary ring of vesicles. In two weeks the lesion no longer protruded. April 21, 1930, the lesion of the back had disappeared. June 2, 1930, there

was a tiny scab over this site. October 1, 1930, there remains slight thickening only at the site of the former back lesion. The exact pathology of the lesion is not known.

This is undoubtedly a case where the amount applied was too small and where a second application would have been preferable.

CASE VII.—*Senile Warts*.—M. L., female, aged fifty-six, came to Memorial Hospital April 24, 1929, for treatment to several keratoses and senile warts scattered over the integument. Her skin appeared much older than her age would indicate, possibly due to a very early menopause. Many lesions were treated with X-ray and most disappeared, but a large one 2.5 centimetres in diameter in the abdominal wall persisted.

June 2, 1930, to this lesion was applied  $\frac{1}{2}$  minim of 10 per cent. mustard-gas solution.

June 23, 1930, the lesion had reduced one-half in size. September 16, 1930, the lesion is entirely gone and the skin is pliable. No evidence of recurrence.

CASE VIII.—*Pigmented Nævus*.—J. DiP., male, aged twenty-eight, came to the Memorial Hospital June 2, 1930, having a pigmented nævus of the right lumbar region. It was a small purple lesion, elevated and hard.

June 3, 1930, 4 drops of mustard-gas solution were applied; within forty-eight hours there was tremendous vesiculation over the lesion and surrounding skin. September 10, 1930, the lesion is entirely gone.

CASE IX.—*Carcinoma of the Penis*.—A patient of Dr. Archie Dean. One application of mustard gas was made. One week later amputation of the penis was performed. A study of the section of the tumor showed complete destruction of the local disease by necrosis.

CASE X.—A patient of Dr. Archie Dean. This lesion was treated similarly to the above lesion except that the dose of mustard gas was slightly larger. Amputation was performed one week later. Sections of this tumor were more striking than in the first patient with penile cancer. The agent had penetrated the connective-tissue plains between bundles of fascial and muscular tissue, destroying tumor cells which had invaded these layers.

Two cases were next selected with cancer of the penis, to be treated by the mustard gas alone without amputation. These cases were managed and the treatment with the agent carried out by Dr. Russel Ferguson. Both cases were selected (a) having no penetration of the fascia by the neoplasm; (b) having no demonstrable metastases; (c) both being squamous carcinoma, Grade I, radioresistant.

CASE XI.—Patient had a lesion 2.5 by 3 by 1 centimetre thick. Frequent applications were made to the lesion of small doses of the mustard gas. The tumor has been destroyed gradually, and at present, four months after beginning treatment, there is no evidence of disease and there is good normal healing over the site of the original ulcerated tumor.

CASE XII.—The patient had a smaller growth of the penis measuring 1 by 1.5 centimetre by 6 millimetres thick. This was treated by a single large application of the mustard gas. The growth had recurred following external radiation elsewhere, three months previously. It is now five months since the treatment here in Memorial Hospital; there is no evidence of recurrence; and there is normal epithelium over the original site.

#### CONCLUSIONS

(a) *Animal Experiments*.—1. Tar cancers in mice may be controlled by the surface application of mustard gas in absolute alcohol. The action of this chemical produces a severe local reaction, which is slow in healing. It has been found that it is necessary to cover the entire growth completely by the solution, otherwise adjacent untreated portions of the cancer will continue to grow.

2. The removal of a tar cancer in mice by mustard gas does not prevent

## MUSTARD-GAS TREATMENT OF CANCER

the later development of a similar tumor in an adjacent portion of the tarred area of the skin.

3. The presence of a relatively thick mass of tumor tissue on the surface of the body tends to lessen the general toxic reactions that result when mustard gas is applied to the surface of the growth. When the chemical is applied to ulcerating or bleeding areas of a surface growth the resulting toxic reactions usually result in the death of the animal.

4. Studies of the effect of mustard gas on the tongue and the inner surface of the cheek show that the action of the chemical is local and that the absorption of the liquid by the tissues is accomplished within a few seconds. There was no spreading of the action from the tongue or the cheek to other regions of the mouth in immediate contact with the treated surfaces. The doses used in the mouth did not result in destructive changes in the lungs.

5. Mustard gas on the bladder and rectal mucosa produced clear-cut local destruction of the epithelial surfaces of these organs.

(b) *Experiments on the Human.*—1. This report covers cases of skin cancer which are free from recurrence for several months following the application of mustard-gas solution.

2. In these lesions, especially squamous carcinoma, it may be necessary to make more than one application of the mustard-gas solution to effect a complete destruction of the lesion.

3. In the lesions injected intratumorally care and judgment must be exercised as the agent produces such intense inflammatory reaction that great destruction of vital parts may follow.

4. We believe that mustard-gas solution offers another agent for fighting cancer provided the lesion is localized. It is suggested that in a case of neurogenic sarcoma recurrent four times a cure may have been obtained by one interstitial injection of this agent.

# ANIMAL TUMORS AS THERAPEUTIC REAGENTS

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THE recent increase of interest in the investigation of cancer, which is probably largely due to the activities of such organizations as the American Society for the Control of Cancer, has led to the announcement, largely by inexperienced investigators, of a great variety of cancer cures. Such attempts to cure cancer are usually supposed to have a physiological or pathological basis, in contradistinction to the quack variety of cure which is either a matter of absolute deception or some type of caustic substance applicable only to superficial growths. Such caustics can unquestionably cure superficial cancers, but their use has been abandoned by the profession because superior results are obtained by means of surgery and radiation.

Most of the alleged cures brought forward by the profession have therefore an apparent scientific basis. Some of them are in conception imitations of the well-known methods of bacteriology in which the injection of an antigen in animals produces an anti-serum. The serum so obtained is used in a therapeutic way. Most of the other varieties have been the employment either of autolytic products of tissues, embryonic or adult, the blood of newborn children on the admirable *nonsequitur* that as children never have cancer there must be some immune substance in the blood, neither of which assumptions is true; or, finally various products isolated from the organs of internal secretions. Such organ products may be either of normal glands or from animals which have been treated in a variety of ways, such treatment being supposed to stimulate the endocrine organs, either by making them secrete more actively or by altering them in some fashion so as to give them powers which they do not possess under normal conditions.

One of the first to attempt to obtain a cancer anti-serum was Jensen, who shared with Leo Loeb the initiation of the active experimental era of cancer investigation by showing that tumors arising spontaneously in animals of certain species could be transplanted easily. Fortunately these animals were the albino mouse and rat; hence easily handled and inexpensive to keep. Successful transplantation of the neoplasms of larger mammals has not yet been accomplished, though grafting of dog tumors has been tried since 1804. Possibly if a large number of young dogs were available, such transplantation would be successful, but even with mice and rats it is a common experience that the first inoculations in a primary tumor take in only a small per cent. often only two or three. The use of this number of dogs would be obviously limited to laboratories of large financial resources.

Jensen injected rabbits with tumor material from albino rats and treated

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tumor-bearing animals with the serum so obtained. He saw what he thought was an effective cure, but being a careful observer repeated his experiments and studied a large series of control animals, so that finally he was forced to the conclusion that the serum had little or no effect and that the apparent cures of transplanted tumors were due to spontaneous disappearance and not to the effect of the serum, as originally had been imagined.

These careful experiments apparently have never penetrated the literature of cancer, for they have been repeated over and over again by numerous investigators with negative results.

Those who have made therapeutic claims have rarely offered evidence that they knew the rate of disappearance, in untreated animals, of the tumor with which they worked.

The most important repetition of this work is due to Lumsden, whose numerous papers are summarized in the *Report* of the International Congress on Cancer in London in 1928, page 216. Lumsden found that by inoculating rabbits with mouse cancer it is possible to produce not only a general anti-mouse group of bodies which are not specific against cancer cells, but also believes he has obtained another group of antibodies toxic not only to mouse-cancer cells which were used as an antigen, but also damaging to many other varieties of malignant cells. He found also that the anti-sera made in sheep or in rats are more specific than those made in rabbits. Again, if human cancer is injected into a sheep, the sheep's serum is capable of killing cultures of mouse carcinoma or rat sarcoma, whereas the normal cells in the culture are not damaged. If such serum is injected into the leg of an animal bearing a tumor, and the circulation is slowed up by a temporary ligature, the tumor recedes, and this recession is inevitably followed by a recession of an untreated tumor of the other leg. The injection into the general circulation of such a serum is not effective, probably because of the protective action of the liver, which seizes upon foreign proteins and rapidly removes them from the general circulation. Lumsden is careful to point out that his work does not necessarily imply that the treatment would be effective on spontaneous tumors, for while he feels certain that an animal can be made to form antibodies against implanted homologous tumor cells, it cannot do so against autologous malignant cells.

Lumsden's results have been carefully controlled and are the best which have appeared on this subject of the action of an anti-cancer serum.

Attempts to produce cures, either in man or animals, by the direct inoculation of either a portion of autologous tumors or by various preparations of tumors arising in other animals, have regularly failed. The killing of tumors by trituration, radiation, or by chemicals, and the injection of material so obtained in man or animal, has not so far succeeded. The same is true of various other preparations, such as autolytic products from fetal cells, and so forth. The only fact which has been observed is that in some animal tumors—though not all—a tumor which grows and then spontaneously recedes leaves the animal immune to further inoculations. But it is

important to remember that this is not a general phenomenon, and there are some tumors in which such a sequence of events is not observable. So, too, if living cells of a great variety, blood, crushed tissue, particles of organs, and so forth, are injected into an animal, that animal becomes immune to the inoculation of a tumor, but not immune to the spontaneous appearance of a tumor; nor can such immunity against grafting be obtained in all tumors. There are highly virulent mouse and rat tumors which resist such immunity. The explanation of this phenomenon has not yet been offered. It is probable that the processes which precede the taking of the grafted tumors are very delicate and that a very small degree of immune reaction, when acting upon the implanted cells which are not yet fully nourished by necessarily newly formed capillaries, will be effective in the prevention of grafts, while it will not be effective in the destruction of an already growing tumor.

Much criticism has been made of the use of grafted tumors as a means of studying not only the biology of tumors but of testing the effect of therapeutic agents. Indeed, one prominent surgeon goes so far as to say that nothing of value has been learned in the last thirty years by the application of the experimental method to grafted tumors. It is not necessary to discuss here such an absurd statement, which is equivalent to denying any progress based upon bacterial cultures, because the cultures are not the disease, but there is an element of truth in some of the criticisms which have been made. These are based upon the enormous amount of absolutely contradictory work which has been published, and the reason for this contradiction is the lack of care on the part of the investigators in controlling their results and in generalizing from a single type of tumor. Only those who are familiar by long study with the vagaries of implanted tumors, due largely to extraneous circumstances, realize the pitfalls of the experimental methods. The use of a tumor which disappears in about 50 per cent. of the animals used would hardly be a logical basis for the announcement that a drug could cure cancer if the number of cures produced by the drug were identical with the spontaneous disappearance rate; yet such a statement has been published. Unfortunately there are very few rat tumors which do not from time to time show such extraordinary variation in their growth capacity or in the resistance of the host. Apparently such small matters as diet and the general health of the animal may play a part in such disappearance. But there are certain mouse tumors which do not disappear spontaneously, though they have been observed through many thousands of inoculations over a period of fifteen years. These tumors do not immunize against themselves and hence are just as valuable a test material as a spontaneous tumor. When such tumors are used, all the alleged cures fail. No elaborate statistical computation has to be made if this tumor has been used to decide whether the resulting disappearance is due to an interreaction between the host and the tumor, or whether it is due to an agent which is supposed to have therapeutic activities.

Using such a tumor, we can draw pretty shrewd conclusions as to the value of therapy, and it should be from a humanitarian standpoint a matter of

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compulsion that before an alleged cure is trumpeted by the newspapers, or even presented before a medical society, with the resulting inevitable disappointment and misery which ensue upon any such publicity, the alleged therapeutic substance should be tried out under the conditions outlined.

If any agent will cure, for example, 50 per cent. of the Crocker Fund mouse sarcoma 180, it will cure human cancer. Using this tumor, the colloidal lead of Blair Bell was shown not to be effective as a cure. It will therefore probably not be effective in any large per cent. of human tumors except in some which for unknown reasons seem to be easily poisoned by the lead. Nevertheless, of the many hundreds of substances tested in the Crocker Laboratory, the original Blair Bell colloidal lead is far more destructive of tumor tissue than any other substance investigated. Only a thin sheath of tumor cells remains at the periphery of the tumor after the injection of a suitable dose of colloidal lead. All the other preparations of lead used have shown themselves to be less effective in such destruction. Colloidal gold scarcely damages the tumor at all; but I am speaking not of the commercial gold which is sold about the country at an exorbitant price and which contains only a trace of gold, but of a laboratory colloid which contains large quantities of the material.

All the sera, all the adrenal cortices, all the other alleged cures or alleged treatments, have failed to influence this tumor. It is curable by surgery in the early stages before metastasis takes place. It can be cured by thrombotic agents, such as a  $\frac{1}{2}$  per cent. solution of zinc chloride, provided the mouse is protected by preliminary injection of adrenalin around the tumor. It can be cured by certain of the quack caustics which destroy tissues by their corrosive action, provided metastasis has not taken place. It can be cured by sufficient doses of radium or X-ray. It therefore resembles very closely a human malignant tumor and offers a simple method of preliminary check on any therapeutic method.

Another phase of therapy of animal tumors has been valuable. The early quantitative work was begun by Mottram and Russ of the Middlesex Hospital about the same time as Wood and Prime were carrying on a long series of studies of exposures of tumors and normal tissue to radium and X-ray. The experimental proof of the large doses of X-ray or radium necessary to kill all the cells of a rapidly growing animal tumor was received by those who were practicing therapy with extreme incredulity if not absolute denial of the significance of the observations. When the experiments were repeated by some of the German workers, extraordinary pronouncements were printed, practically stating that it was impossible to cure an animal tumor with X-ray. Some of these discrepancies were due to the fact that the Germans did not take into consideration the scatter which is entirely absent when small particles are rayed, unless they are placed upon heavy wooden supports or other sources of secondary radiation. As this scatter has been found to add as high as 50 per cent. to the dose, it is easy to see that very long exposures are required under these conditions. A good summary of the subject has



recently been published by Krebs in the *Acta Radiologica* as Supplement VIII, 1929. But while these original experiments were published more than ten years ago, they have not yet received general acceptance by the practitioner. The careful measurements of X-ray and radium made possible only in the last few years have forced the conclusion that the statement made fifteen years ago that three to seven skin erythemas, depending on the tumor, are required to kill all cells of an animal tumor, are exactly true of most of the human tumors. Indeed, very interesting observations have recently been published by Martin and Quimby of their work at the Memorial Hospital in studying the end-results of the treatment of carcinoma of the mouth, in which they have shown that unless eight or ten skin erythema doses are applied to the tumor cells, a cure will not be obtained. The same observation has been made on the cervix where, owing to the anatomical independence of the uterus from other organs, it is possible to put in very heavy doses of radium; that many have been using ten to twenty erythema doses to destroy the cells of the cervical carcinomata and even under these circumstances have had to acknowledge that occasionally they have failed to have success even though the growth was restricted in its distribution.

The Regaud school have come to the same conclusion and are giving to tumors of the tongue and the metastases in the nodes equivalent to eight erythemas in ten to fifteen days. With such heroic doses, using high filtrations such as two millimetres of copper or two millimetres of zinc, they are accomplishing results which they could not achieve with lower degrees of filtration and shorter time. The explanation is probably due to the prolongation of the exposure period, and as they apparently use either a radium pack or X-ray interchangeably on this type of treatment, it is presumable that the highly filtered X-ray and the highly filtered radium are clinically equivalent. That they are biologically equivalent has been shown by Wood on tumors and Packard on drosophila eggs.

While all these results have been immensely discouraging to those who have attempted to cure cancer with radiation, they have pointed the way for real therapy as distinguished from temporary palliation. They have taught us the necessity of massive doses and the dangers of repeated divided doses of low voltage X-ray, which merely produces damage to the tissues, atrophies the blood-vessels, and, as a sufficient quantity is not administered to the deeper tissues, destruction of a large proportion of the tumor cells does not take place.

The next step will be the combination of one or more chemo-therapeutic agents with the radiation, so that the cells are damaged by the serum chemically and at the same time receive additional damage from the radiation. Whether such a combination will bring any effective control over such a multifarious disease as cancer, is a matter for future investigators to determine.

# MECHANISMUS DER METHYLENBLAUATMUNG

VON OTTO WARBURG, M.D.

VON BERLIN-DAHLEM

ZELLPHYSIOLOGISCH betrachtet unterscheiden sich Tumorzellen von den normalen Zellen durch ihre gestörte Atmung. Wird die Atmung von Körperzellen gestört, so ist die Regel, dass die Zellen zugrundegehen. Gehen die Zellen nicht zugrunde, sondern teilen sie sich trotz der Atmungsschädigung weiter, so giebt es zwei Möglichkeiten: entweder die Atmungsschädigung verschwindet wieder im Lauf der auf sie folgenden Teilungen. Dann hat man zwar ungeordnetes Wachstum (z B Granulome), aber keine Tumoren. Oder die Atmungsschädigung verschwindet nicht im Lauf der auf sie folgenden Teilungen, die Atmungsschädigung wird vererbt von Zelle zu Zelle. Dann hat man Tumoren. Dies ist keine Theorie, sondern eine Zusammenfassung der vorliegenden Stoffwechselfmessungen. Es giebt im Körper höherer Tiere keine von Zellteilung zu Zellteilung persistierende Atmungsschädigung, ausser in der Zellen der Tumoren.

Bei dieser Sachlage erscheint es wichtig, Wirkungen näher zu untersuchen, mit denen man die Atmung lebender Zellen steigern kann. Ueber eine solche Wirkung und ihre chemische Erklärung sei hier kurz berichtet.

Barron und Harrop haben gefunden, dass die Atmung kernloser roter Blutzellen (Mensch, Hund, Kaninchen) auf das 10- bis 20-fache steigt, wenn man in sie eine minimale Menge Methylenblau hineinbringt. Nach Versuchen des Verfassers mit F. Kubowitz und W. Christian liegt bei der Methylenblau-Atmung eine gekoppelte Katalyse vor, bei der die Verbrennung der organischen Substanz, wie bei der Sauerstoffatmung, durch die katalytische Wirkung einer Eisenporphyrinverbindung hervorgebracht wird.

Bringt man Methylenblau in rote Blutzellen, so oxydiert das Methylenblau zweiwertiges Haemoglobineisen zu dreiwertigem Methaemoglobinoisen, während es selbst in Methylenweiss übergeht:

Methylenblau + Haemoglobin = Methylenweiss + Methaemoglobin (1).  
Das so gebildete Methaemoglobin oxydiert in der Zelle Zucker oder dessen Spaltungsprodukte zu Brenztraubensäure, Kohlensäure und Wasser, unter Rückbildung von zweiwertigem Haemoglobineisen. Auf (1) folgt.

Methaemoglobin + Zucker = Haemoglobin + Oxydationsprodukte des Zuckers (2) und ausserdem bei Gegenwart von Sauerstoff.

Methylenweiss + Sauerstoff = Methylenblau (3).  
sodass also eine minimale Menge Methylenblau beliebige Mengen Zucker auf dem Weg über die Haemoglobinoxidation verbrennen kann. Nach ihrem chemischen Mechanismus ist die Methylenblauatmung eine gekoppelte Katalyse: Methylenblau oxydiert das Blutfarbstoffeisen katalytisch, das Blutfarbstoffeisen oxydiert den Zucker katalytisch.

Ist dies richtig, so muss es möglich sein, die Erscheinung der Methylenblauatmung auch ohne Methylenblau hervorzurufen, indem man Methylenblau durch andere Methaemoglobinbildner ersetzt (die allerdings die Zellen nicht schädigen dürfen). Ein für unsre Zwecke geeigneter Methaemoglobinbildner ist Amylnitrit. Setzt man Amylnitrit zu roten Blutzellen, so wird das zweiwertige Haemoglobineisen in das dreiwertige Methaemoglobineisen verwandelt. Fügt man Zucker hinzu und bringt die braunen Methaemoglobinzellen in den Brutschrank, so sieht man, wie das Methaemoglobin in kurzer Zeit von dem Zucker reduziert wird. Wie bei der Methylenblauatmung entstehen als Endprodukte der Oxydation Brenztraubensäure, Kohlensäure und Wasser. Dabei wird die vorher braune Zellsuspension, wenn sie mit Luft gesättigt ist, ziegelrot (Farbe des Oxyhaemoglobins), wenn sie mit Kohlenoxyd gesättigt ist, kirschrot (Farbe des Kohlenoxydhaemoglobins). Ohne Zucker bleibt die Zellsuspension braun. Wegen der Schnelligkeit der Reaktionen und wegen der leicht erkennbaren Farbänderungen eignet sich dieser Versuch als Demonstration in der Vorlesung.

Die hier nur angedeuteten Experimente erklären die von Ehrlich vor vielen Jahren entdeckt "vitale Methylenblaureduktion." Ueberall, wo Atmung ist, findet man, wenn man den Sauerstoff abschliesst, Methylenblaureduktion. Ueberall, wo Atmung ist, hat man bei Abschluss von Sauerstoff zweiwertiges Eisen, nämlich das zweiwertige Haemineisen des Atmungsferments. Da nun zweiwertiges Haemineisen, wie die Versuche mit roten Blutzellen lehren, Methylenblau zu Methylenweiss reduziert, so müssen alle atmenden Zellen bei Abschluss von Sauerstoff Methylenblau reduzieren. Es müssen ferner bei der Methylenblauatmung dieselben Oxydationsprodukte entstehen, wie bei der Sauerstoffatmung, weil der Mechanismus der Oxydation in beiden Fällen identisch ist. In beiden Fällen ist die Oxydation der organischen Substanz eine Oxydation durch Haemineisen. Methylenblau ersetzt also nicht etwa den Katalysator der normalen Atmung, das Haemineisen, sondern es ersetzt nur den Sauerstoff. Bei der Sauerstoffatmung oxydiert der Sauerstoff das Haemineisen, bei der Methylenblauatmung oxydiert das Methylenblau das Haemineisen.

Die theoretischen Grundlagen der hier besprochenen chemischen Reaktionen findet man in den Arbeiten von Conant und Fieser sowie von Mansfield Clark.

# III

REGIONAL CANCER

- DEAN LEWIS, M.D. Baltimore, Md.  
Professor of Surgery, Johns Hopkins Medical School.  
"Elephantiasis Nervorum."
- PIERRE MASSON, M.D. Montreal, Canada  
Professor of Pathology, University of Montreal.  
"Giant Neuro-Nævus of the Hairy Scalp."
- MAX CUTLER, M.D. New York, N. Y.  
Formerly Director of Cancer Research, New York City Cancer Institute.  
"Transillumination of the Breast."
- JOSEPH COLT BLOODGOOD, M.D. Baltimore, Md.  
Clinical Professor of Surgery, Johns Hopkins Medical School.  
"Border-line Breast Tumors."
- BURTON J. LEE, M.D. New York, N. Y.  
Clinical Director of Memorial Hospital.  
"Cystosarcoma Phyllodes Mammæ."
- BERNARD F. SCHREINER, M.D. Buffalo, N. Y.  
Surgeon to the State Institute for the Study of Malignant Disease.  
"The Results of Treatment of Cancer of the Breast; Based on a Study of 489 Cases, 1914-1925."
- M. LENZ, M.D. New York, N. Y.  
Director of Radiology, Montefiore Hospital.  
"Metastases to the Skeleton, Brain and Spinal Cord from Cancer of the Breast, and the Effect of Radiotherapy."
- JOHN M. T. FINNEY, M.D. Baltimore, Md.  
Clinical Professor of Surgery, the Johns Hopkins Medical School.  
"Papilloma of the Duodenum. Report of Case Diagnosed Pre-operatively."
- RAPHAEL BASTIANELLI, M.D. Rome, Italy  
Professor of Surgery, University of Rome.  
"Cancer of Perigastraduodenale."
- EVARTS T. GRAHAM, M.D. St. Louis, Mo.  
Professor of Surgery, Washington University, School of Medicine.  
"The Prevention of Carcinoma of the Gall-Bladder."
- HOWARD A. KELLY, M.D., LL.D. Baltimore, Md.  
Emeritus Professor of Gynecology, Johns Hopkins Medical School.  
"Electro-Surgery in Gynecology."
- BENJAMIN S. BARRINGER, M.D. New York, N. Y.  
Attending Urologist to Memorial Hospital and Fifth Avenue Hospital.  
"Carcinoma of the Prostate."
- HARRY C. SALTZSTEIN, M.D. Detroit, Michigan  
Member American Society of Control of Cancer.  
"Some Commoner Difficulties in Diagnosis and Treatment of Carcinoma of the Rectum and Colon."
- ERNEST A. CODMAN, M.D. Boston, Mass.  
Former Registrar of the American Bone Sarcoma Registry of the American College of Surgeons.  
"The Pathology Associated with Rupture of the Supraspinatus Tendon."
- CLAUD REGAUD, M.D. Paris, France  
Director of the Radium Institute of the University of Paris.  
"Une Variété Histologique D'Epithelioma Du Col De L'Uterus."

## ELEPHANTIASIS NERVORUM

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IN THE laboratory of Surgical Pathology of the Johns Hopkins Hospital tissue may be found which has been removed from seventeen cases of multiple neurofibromatosis. In four cases the tumors developed upon a circumscribed area of distribution of a nerve. The general and localized forms are much the same histologically and can possibly be best grouped under the term elephantiasis nervorum. In 1891, Bruns analyzed forty-two cases of so-called *Rankenneurom* or plexiform neuroma which had appeared in the literature, and reported the findings in eight cases observed by himself. The fusiform or nodular strands of tissue which were imbedded in soft, succulent, interstitial tissue represented thickened and elongated nerves in a circumscribed area of the subcutaneous tissues and skin. The nodular thickening of the nerves was caused by a connective-tissue growth of the nerve sheath, the perineurium and endoneurium. With the stains then at command, no new formation of neurofibrillæ could be made out. Neurofibrillæ may be demonstrated passing through such growths, but they probably are not newly developed and cannot be regarded as taking any active part in the formation of the growths occurring on the nerves. Bruns states in his article that the origin of these tumors and their relation to other tumors developing upon nerves are of the greatest interest. He believed that they represented a form of congenital elephantiasis, if by this term may be understood a congenital anlage, predisposing to tumor-like connective tissue growths which involve the skin and subcutaneous tissues, affecting sometimes the blood-vessels; at other times the lymphatic vessels; and still at other times the nerves—elephantiasis telangiectodes—lymphangiectodes and neuromatodes. If the nerves are affected, the term elephantiasis neuromatodes might be employed. The Rankenneurom or plexiform neuroma should be considered as a form of congenital elephantiasis. In this type of tumor a limited part of the nerve is involved. As the result of connective tissue growth the nerve becomes thickened and elongated. These growths differ in form, only, from the multiple fibromas of the skin and nerve trunks observed in von Recklinghausen's disease. They are essentially of the same nature. The plexiform neuroma and the multiple neurofibromata are congenital. Sometimes there is a history of a hereditary tendency. They are frequently multiple and of the same histologic structure. Bruns groups, therefore, under the term elephantiasis nervorum the so-called general neurofibromatosis, plexiform neuromas, in which the tumors develop upon the circumscribed area of distribution of the nerve, and those tumors developing on the terminal distribution of cutaneous nerves—fibromata mollusca.

Five of the seventeen cases previously referred to were cases without deep nerve tumors. Eight cases had deep nerve tumors; in four cases the tumor occurring upon the deep nerves was malignant; in four cases benign. Of the four benign tumors one occurred upon a peripheral nerve, two upon cranial nerves within the skull, and one occurred upon a nerve in the spinal canal. In three instances the tumors were not general, and in still another case the lesion presented was that of a localized cutaneous neurofibromatosis.

Those cases without deep nerve tumors are not of any great interest and



FIG. 1.—Prominence of thigh indicates position of a sarcoma developing in neurofibromatosis.

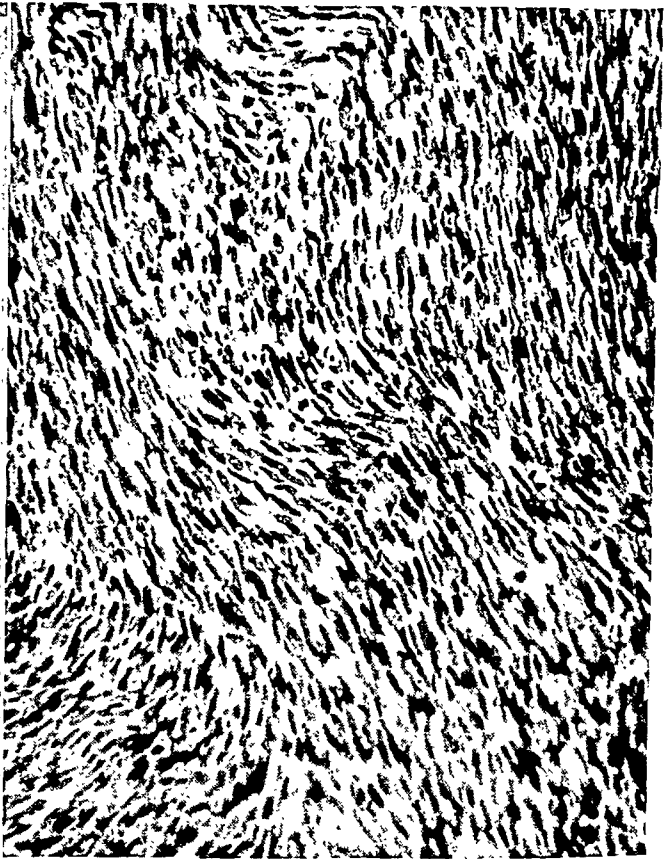


FIG. 2.—Section of tumor which rapidly recurred after partial removal of the tumor seen in Fig. 1.

will be dismissed without much discussion. The superficial tumors were in some cases scattered indiscriminately over the body. In some cases, however, there was a linear and symmetrical distribution. Frequently the tumors reached a certain size and then ceased to grow. Other tumors might appear *de novo*, or might develop from a minute nodule which had been previously discovered. In one case 118 tumors were removed at the request of the patient for cosmetic reasons.

Patients with elephantiasis nervorum seem to be especially disposed to malignant degeneration of the tumors which develop in the nerves. The predisposition to malignant degeneration seems to be more marked in the

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general than the localized form. Perhaps I have not enough cases upon which to base such a statement, but malignant changes were not observed in the localized forms.

*Elephantiasis Nervorum with Deep Nerve Tumors.*—CASE I.—G. B., white male, aged twenty-eight years. This patient was first admitted to the Medical Service during August, 1920. He stated that he had had lumps all over the body since early childhood. The one behind his right ear was noted by his mother when he was one year old. New lumps appeared from time to time. They frequently ceased to grow, but did not disappear. These are not painful or tender. In 1918 a tumor behind the right ear was excised, and a tumor on the left leg partially removed. The patient was again in the hospital on August 8, 1926, when a small tumor was removed from the left side of the chest. This was diagnosed as of the type occurring in von Recklinghausen's disease. Recently there has been some stiffness of the left knee and disturbance of function of the left leg. This is due to a large, pedunculated tumor which has been present for fifteen years, but which recently has grown large and hangs down over the knee.

An examination reveals numerous small tumors over the body. A large, soft, boggy mass is present in the anterior part of the left thigh, which extends from just below Poupart's ligament downward and hangs over the knee. The overlying skin has a soft, elastic texture. Palpation of the tumor suggests a fluid wave. The patella is located in this mass of tissue.

October 4, 1926, an operation was performed. A large cavity was found in the tumor which communicated with the joint. When this was opened about 800 cubic centimetres of fluid were evacuated. The tumor seemed to infiltrate the muscle. The patient returned in January, 1929. A large mass had developed over the left side of the pelvis just above Poupart's ligament. Examination revealed a large, hard mass just above Poupart's ligament which extended to the umbilicus and caused some protrusion of the abdominal wall. The tumor is stony hard in consistence and apparently extends into the pelvis. Loops of intestine seem to lie over it. The mass in the leg is much smaller than when the patient was last in the hospital.

January 19, 1929, a biopsy was performed. Part of the tumor was removed without opening the peritoneal cavity. The tumor was firm and fibrous in character. A diagnosis of spindle-cell sarcoma was made.

Since the above diagnosis was made the patient has been getting radium treatments which have so far not affected the size of the tumor.

CASE II.—E. H., white female, aged fifty years. *Diagnosis.*—Sarcoma in soft parts of left hip. Since childhood the patient has had drawing pains in the left leg and thigh. She had worn red flannels and massaged the lower extremity because of these pains. Curious pigmented spots and blotches were distributed over the trunk, abdomen and extremities. Since childhood numerous painless, slightly firm, subcutaneous nodules have been noted on the lower extremities. These have increased only slightly in size, and at the present time measure from 2 to 6 centimetres in diameter. The pains in the left leg have been more severe during the last ten years, and the difficulty in lifting and flexing the left leg and thigh has been more pronounced. Five or six years ago she noticed that the left hip seemed slightly larger than the right one. A definite enlargement has been noted for a year. The tumor was operated upon one year before admission to this hospital. It was attached to the sciatic nerve, and could not be entirely removed. Since this incomplete operation the tumor has increased rapidly in size in spite of radium treatment. The pain has been so severe that narcotics were required. Hearing is impaired in the right ear. Patient complains of numbness on the right side of face. The diagnosis of malignant degeneration of a tumor in general neurofibromatosis was made. December 11, 1922, an attempt was made to remove the large tumor in the sciatic nerve. The patient died on the day of the operation.



A pathological diagnosis of spindle-cell sarcoma with extensive necrosis and degeneration was made.

CASE III.—J. W., white female, aged thirty years. Two years before entering the hospital the patient noticed a tingling sensation in the right leg and sometimes a sharp, stabbing pain around the right knee. Six months ago she first noticed a lump in the back of the right thigh just above the knee. This gradually increased in size and the tingling and burning sensation in the leg became more severe. No motor disturbances noted. The patient states that she had observed numerous small tumors over the body for years.

Examination revealed slight fulness on the posterior surface of the right thigh just above the popliteal fossa. This fulness is caused by a hard, lobulated, egg-shaped mass 6 centimetres in length, which lies between the hamstring tendons. Pressure causes pain in the tumor and along the outer side of the calf and heel. Sensation is slightly impaired. On the left side the foot is clubbed. On the anterior surface of the trunk are numerous soft, slightly elevated tumors which measure 1 to 3 centimetres in diameter.

On January 25, the tumor, which was firmly adherent to the popliteal nerve, was excised. It is stated in the history that this tumor was so intimately connected with the external popliteal nerve that some fibres of the nerve had to be divided when the tumor was removed. The tumor was circumscribed, measuring 5 centimetres in its longest diameter; 3 centimetres across.

This patient is reported as having died November 11, 1919, of sarcoma. The diagnosis made of the tumor which was first removed was fibromyxoma.

CASE IV.—C. M., white male, aged twenty-six years, was admitted to the hospital during April, 1922. The symptoms began two years before admission. A diagnosis of static flat-foot and Morton's disease was made soon after the onset of symptoms. The pain passed up the left foot along the leg as high as the knee. He returned to the dispensary in April, 1922, complaining of pain and swelling in the left thigh. He gave the history that two years before he accidentally struck his hand against the left buttock and noted a tender spot. No tumor could be palpated. Some weeks later he noticed a small, hard nodule beneath the skin. This was about the size of the end of his finger. The lump gradually increased in size and has remained sensitive to trauma. At about the same time he noticed a swelling which was entirely distinct from the one felt posteriorly. Both tumors have increased in size.

On the anterior surface of the left thigh is a deeply located tumor which begins about 15 centimetres below the anterior superior spine and is about 18 centimetres wide and 22 centimetres long. It is not tender on pressure; is elastic, but does not pulsate. Multiple fusiform tumors are scattered over the body just beneath the skin.

Another mass, measuring 16 centimetres in each direction, begins at the left gluteal fold and extends downward on the posterior surface of the thigh. This mass is freely movable. The skin over it is normal and on palpation this mass is quite sensitive. Several chains of nodules can be palpated along the anterior and posterior surfaces of the forearms, and another chain, which extends along the internal surface of the arms into the axilla can be felt. This arrangement suggests a plexiform neuroma. Dark brown, pigmented areas varying in size from freckles to spots, measuring 6 centimetres in diameter, are scattered over the body and extremities. An operation was performed April 11, 1922, for removal of the tumor lying posteriorly. The fibres of the sciatic nerve were separated by the tumor. A line of cleavage between the tumor and nerve was found. The tumor was removed from the nerve, some of the capsule being left behind. The tumor on the anterior surface of the thigh was connected with the femoral nerve, and it was necessary to divide some of the nerve fibres running into the tumor, which was then enucleated in one mass.

The pathological diagnosis was fibromyxoma (benign) of the nerve sheath.

The following note is found on the history: "July, 1922, the patient has a recurrent

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sarcoma of the left thigh. Pathological study reveals that this tumor is very cellular and malignant."

The questionnaire was returned unanswered, so the ultimate result cannot be determined.

CASE V.—The history of the following case will be given because the specimen illustrating the structure of this tumor will be reproduced. This patient is a white man, aged twenty-one, who has tumors symmetrically distributed over the body. One tumor on the outer side of the left arm about the middle is larger than the others. Some eleven years ago he discovered by accident a mass upon the inner aspect of the right arm. Since that time numerous other small nodules have appeared over the entire body. Recently there has been considerable pain in the tumor on the outer side of the arm which has radiated over the distribution of the radial nerve. Scattered over the body are numerous well-circumscribed tumors of varying size. The greater number are about the size of a pecan. Most all are superficial. They are firm, somewhat rubbery in consistence, and in general follow the distribution of cutaneous nerve trunks. In the left arm along the course of all the radial nerve in the radial groove is a tumor mass, fusiform in shape, constricted near the middle. Pressure on the mass causes tingling over the distribution of the radial nerve. Pigmented areas are also noted in the skin. The tumor of the radial nerve was removed because of the sensation experienced when this nerve was touched or struck. It could easily be enucleated from the nerve.

The patient returned in March, 1930. A tumor was removed from the ulnar nerve on the right side. This tumor, which appeared myxomatous in places, could easily be enucleated. The tumor which had been removed previously from the radial nerve seemed more fibrous structurally.

This case is cited because the histology of the tumor removed from the ulnar nerve will be discussed later.

In the following case the tumors developed upon the nerves in one extremity. The extremity was greater in circumference and in length than the one on the opposite side. A linear distribution of the tumors could be made out. This distribution was most pronounced over the short saphenous nerve and along the posterior tibial nerve as it passed into the foot posterior to the internal malleolus.

CASE VI.—R. W., white female, aged four years. A biopsy was performed September 28, 1928. The following history was given. About sixteen months before admission to the hospital, it was noted that the left thigh and leg were larger than the right. During the sixteen months there has been a progressive, symmetrical increase in the size of the left lower extremity and hip as compared with the right. Thirteen months before admission small, tender, subcutaneous nodules appeared in the region of the head of the left fibula. There has been no pain. The patient favors the right leg somewhat. The nodules have grown slightly.

The left lower extremity and left side of the pelvis are obviously larger than the right. The extremity is symmetrically and smoothly enlarged and the tissues do not appear flabby. The hypertrophy involves all of the tissues from the gluteal muscles to the tip of the toes. There is no difference in muscle power; no limitation of motion, no spasticity or pain. There is some eversion of the left foot. Near the left knee and ankle, both medially and laterally, firm, discrete masses which seem somewhat like strands of hypertrophied muscle may be made out. These nodules appear over the distribution of the short saphenous nerve. The nodules which can be palpated posterior to the internal malleolus are located along the course of the posterior tibial nerve. No asymmetry of the body is noticed elsewhere.

On September 18, 1928, some of the tumors posterior to the internal malleolus were excised. In doing this some of the fibres of the posterior tibial nerve were cut. The nerve was then sutured. The appearance of the masses removed may be seen in Fig. 4.

Another instance of asymmetry associated with multiple tumors of nerves of an extremity will be given.

CASE VII.—A. C., white female, aged fourteen years. When the patient was one and a half years of age the mother noted that the right ankle and foot were larger than the left.

Shortly thereafter it was noted that the entire extremity was larger. The relative difference in size of the two extremities has increased up to the time of admission to the hospital.

The patient, a healthy girl of fourteen, has no abnormality except that of the right lower extremity. This extremity is of greater circumference than the left. It is longer and there is a deformity of the knee and ankle. As a result the patient walks with great difficulty. The weight is borne on the dorsum of a club-foot. A lobulated tumor or tumors may be palpated beneath the deep fascia. There seem to be many tumors. The cylindrical masses, one to two inches in diameter, cause a great enlarge-

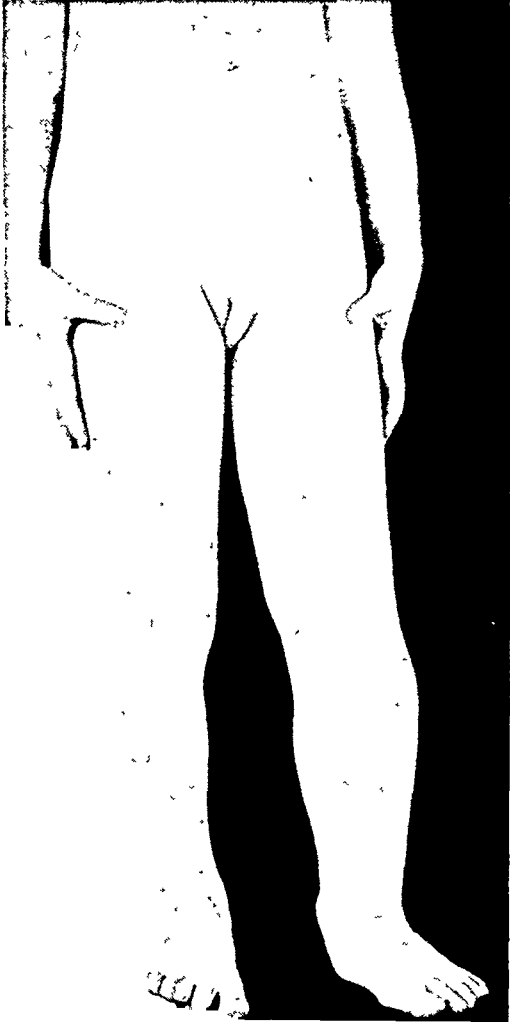


FIG. 3.—Marked enlargement of the left lower extremity with increase in length associated with multiple tumors of the nerves. The situation of some of these behind the internal malleolus is indicated by the prominences.



FIG. 4.—Type of tumor masses removed from the posterior tibial nerve just above the ankle-joint.

ment of the posterior upper two-thirds of the leg and lower part of the thigh. There is distinct tenderness on deep pressure over this region. Measurements indicate that the right thigh is 4 inches larger than the left, and the right calf 3 inches larger. The right lower extremity is 5½ inches longer than the left. The muscle power of the right leg is diminished. An X-ray examination of the bones of the right lower extremity reveals an increase in length, decrease in diameter and structural atrophy.

This patient was on the service of Doctor Willis Campbell, of Memphis, Tennessee,

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who by repeated operations removed many lobulated tumors. The extremity was decreased considerably in size. The femur was then shortened, and later the ankle was stabilized by removing the astragalus and the leg shortened by removing 1 inch of both bones. The lower epiphysis of the tibia was destroyed, but it was thought that the excessive growth in the epiphysis of the other bones would make up for this. After the operations on the soft parts and bone, the extremities were of the same length. The right leg was approximately 1 inch greater in diameter than the left. This patient was reported well on July 17, 1929. Histologically a diagnosis of neurofibromatosis was made.

The tumors which have been reported differ clinically, but are essentially of the same nature structurally. The generalized type, with tumors upon the peripheral nerves, has a marked tendency to malignant degeneration. Those cases in which one extremity has been involved have been characterized by an increase in the diameter and length of the extremity. In the latter group, pigmentation of the skin and fibromata mollusca have not been a part of the clinical picture. Neither have there been changes like those of lobulated elephantiasis which are associated with neurofibromatosis when the superficial nerves are involved.

The tumors upon deep nerves in von Recklinghausen's disease seem prone to undergo malignant degeneration. Excluding three patients who had symptoms associated with an intracranial or intraspinal growth only, sarcoma developed in four of the five cases. One of these tumors was inoperable; the other three recurred following enucleation or resection of the nerve involved. The tumors grew rapidly, early attaining a relatively large size, and recurred soon after attempt at removal. The tendency of these tumors to become malignant has been emphasized from time to time. In 1891 Garré reported seventeen cases in which sarcomas developed in tumors upon the deep nerves in von Recklinghausen's disease. Ten of these developed in nerves of the upper extremity, the median being the nerve most frequently affected. The growth usually extends along the nerve primarily affected, many nodules developing in the nerve. Cases have been noted in which secondary malignant nodules developed in the ulnar, radial or cutaneous nerves of the same side when the primary tumor was situated in the median nerve. In the transition stage between the benign neurofibroma and the sarcoma it may be difficult to state whether the tumor is benign or malignant, even by histological examination. The diagnosis of malignancy is usually not made at operation as there is nothing characteristic enough to warrant such a conclusion, although malignant degeneration of a tumor already present may be strongly suspected. The three cases in which the tumors were localized to an extremity have shown no tendency to malignant change. This is too small a group to justify any conclusion as to the frequency of malignant changes. Structurally these growths are the same as those of the diffuse forms and there is no reason why malignant changes should not occur.

Trauma and incomplete removal have, in a number of cases, been the factors which apparently predispose to malignant change. This change not infrequently occurs after incomplete removal of a tumor which has been diagnosed as benign. There is always a possibility in such cases that

malignant changes have occurred in the portion of the tumor which was not removed. In Case V, two tumors were removed, one from the radial, the other from the ulnar nerve. These were removed because of tingling and pain over the distribution of the nerve and increase in size of the tumor. Incomplete removal should be avoided and repeated trauma prevented, if possible, because of the dangers of malignant changes.

Multiple tumors occur in this disease in the nerves, meninges and central nervous system. The tumors connected with the peripheral nerves differ structurally from the single neuromas occurring in peripheral nerves.

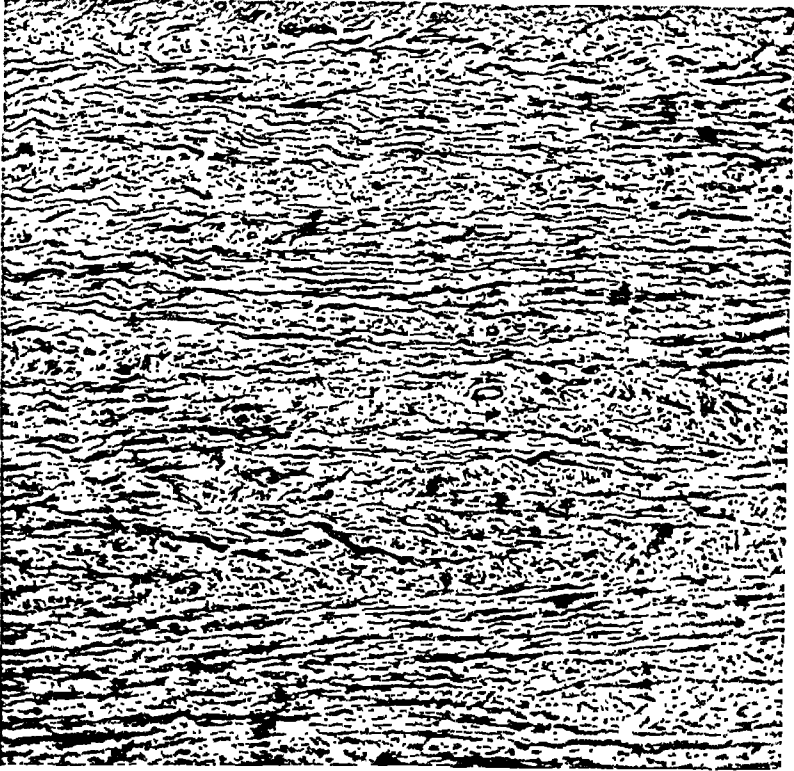


FIG. 5.—Section through one of the tumor masses, removed from Case V showing long connective fibrils. Some of the type B neurinoma tissue is interspersed between these strands.

In earlier times when the tissue composing these growths was described as striated, composed of parallel fibres and fibrillæ, local or regional variations in the histologic picture were considered as secondary. If there was a localized nuclear richness, the tumor was regarded as a sarcoma largely because of the similarity in structure to tumors in other parts which ran a malignant course. The softening with myxomatous degeneration, followed by collections of fluid and cyst formation, was regarded as secondary changes similar to those occurring in other tumors of mesodermal origin.

Verocay was the first to recognize the mixed nature of the tissue found in neurofibromatosis and gave a description of the tissue observed by others before him who failed to grasp its significance. Antoni has shown that the type B tissue, which has a reticular structure without the palisade arrangement

of the cells characteristic of the type *A* tissue, is always present in the tissue occurring in neurofibromatosis (neurofibromas). Many of the tumors occurring in the disease under discussion are apparently pure fibromas. In the central forms of neurofibromatosis pure neurinomatous tissue which occurs in the solitary neuromas may be found. Its occurrence accounts for the relative frequency of central changes in these cases. Penfield states that the tangled or reticular tissue which constitutes the background of all neurofibromas should be considered as a connective-tissue (and probably also a sheath of Schwann) reaction about the fibres of the nerve. Thickening of the nerve trunks, which may be generalized in these cases, is caused by just such a perineuronal hyperplasia of the connective tissue about nerve fibres. When the reaction is marked, a swelling is found on the nerve which must literally be called a tumor, but which, in a strict sense, cannot be called a neoplasm. These tumors differ considerably histologically from the solitary tumors occurring upon peripheral nerves to which the term of neurinoma was given by Verocay. These tumors have but little, if any, tendency to malignancy, as has been recently shown by Lewis and Hart. Penfield agrees with Bielschowsky and Rose that the central changes are regressive ones beginning with adult cells, and points out on the other hand that the same is true in the peripheral nerves. Thus the reactionary and neoplastic process is carried out by fibroblasts which preserve their differentiated characteristics and not by glial cells. The proliferative changes in the fibroblasts in these cases may advance to or pass into the stage of malignancy. This tendency to malignant degeneration in these cases is indicated by the frequency already referred to, in which sarcomas have developed on pre-existing benign tumors. In the growth of the neurofibroma, the reticular tissue, which is supposed by many to be a relative change, is often suppressed. The definite tendency to malignant changes in neurofibromatosis is inherent in the structural changes occurring in the neurofibromatous tissue. The occurrence of ciliated epithelium, as in the tumor described by Garrè, indicates the possibility of the sheath of Schwann contributing to definite structural changes in the tumor.

These tumors differ structurally from the solitary tumors occurring in peripheral nerves which are composed of neurinomatous tissue. This is pathognomonic of a growth which has but little tendency to undergo malignant changes.

# GIANT NEURO-NÆVUS OF THE HAIRY SCALP

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A LONG series of studies on pigmented moles has led me to believe that these tumors are formed essentially by abnormal proliferation of the ends of the tactile nerves. In a general way, this conclusion agrees with that expressed by Soldan in 1899; but it differs in certain essentials. Soldan held that nævi were neurofibromata of the tactile terminations and that, like the "neurofibromata" of the nerve trunks, they were formed by fibromatous proliferation of the connective tissue of the nerves; while I believe that nævi are not connective-tissue tumors at all. In nævi, as in the "neurofibromata" of the nerve trunks, the characteristic element is the syncytium of Schwann, the peripheral neuroglia of Nageotte, emigrated from the neural crest; but, in the nævi, the Schwann cells are partially neurotized. I shall state briefly the proofs that have led me to this conclusion.

The derma of a cellular nævus presents cells of various forms disposed in a constant order. Near the epidermis the cells are rounded, isolated or grouped in columns and more or less pigmented in the different specimens. A little deeper, the cells are more or less elongated like connective-tissue corpuscles; they anastomose with one another and are often grouped in bundles. Among these elongated or round nævus cells, it happens quite frequently that certain cell groups construct more or less typical but very characteristic Wagner-Meissner corpuscles. Careful examination shows that the rounded cells beneath the epidermis are continuous with the nævic tactile corpuscles and these with the more deeply placed elongated nævus cells; and finally that this vast syncytium is continuous with the medullated nerves of the derma. Neurofibrillary impregnations show that the nævus cells are partially occupied by neurites.

If to this group of observations we add that the nævus cells have only a superficial resemblance to connective-tissue corpuscles but that they have all the essential characteristics of Schwann cells, we arrive at the conclusion already stated that nævi are neuromas and neurinomas at one and the same time. Furthermore, the analogies of the superficial rounded cells with the cells of Merkel-Ranvier, satellites of the intra-epidermic ivy-like (*héré-diformes*) endings, those of the nævic corpuscles with Wagner-Meissner corpuscles, leads logically to the conclusion that nævi are neuroneurinomas of tactile nerves.

The specimen, the subject of this paper, was taken at autopsy from a child of three years, who died of bronchopneumonia a few hours after entering the hospital at Strasbourg. The assistant making the autopsy noted a decided elevation of the entire hairy scalp, clearly limited in front, along the sides and behind by the line of insertion of the hair. The hairs were sparse, revealing a white epidermis, everywhere smooth and flat.

## NEURO-NÆVUS OF SCALP

Palpation gave an impression of soft elasticity and vague fluctuation, suggesting phlegmonous infiltration.

Incision revealed an enormous thickening of the derma and of the hypoderm, which were fused together in a perfectly white homogeneous tissue and separated from the epicranium by a thin layer of loose cellular tissue. The fibrous mass measured from 1.5 to 2 centimetres in thickness. In short, it was a generalized and almost smooth pachydermia of the entire hairy scalp. Since it was impossible to remove the whole tumor without mutilation, we were obliged to content ourselves with strips from along the line of incision. The tissue was fixed in Bouin's picro-formol and cut perpendicularly to the epidermic surface. All sections presented the same features.

### HISTOLOGICAL EXAMINATION

*General View.*—One border of the section is formed by normal epidermis, though poor in hair follicles and sebaceous glands. The other border is a thin layer of loose



FIG 1—Nævic tactile corpuscle, apparently isolated in the connective tissue. In reality, this corpuscle is connected by its lower pole with the neuroid bundles. Note the characteristic laminated structure of this corpuscle, which is two or three times larger than a normal Wagner-Meissner corpuscle.



FIG 2—Another example of nævic corpuscle surrounded by fibrous connective tissue. On the left are seen neuroid bundles cut almost transversely and connected by anastomoses. On the right, interlacing of cells (neuroid fibres) without precise bundle formation.

connective tissue. Between the two is the tumor tissue proper, consisting of two layers of almost equal thickness. The deeper layer, containing tiny groups of fat cells, corresponds to the hypoderm; the more superficial layer is compact and corresponds to the fibrous derma. The derma is more or less completely infiltrated as follows: Sometimes the dermal fibrous tissue is recognizable for a certain thickness, sometimes the epidermis is separated from the tumor only by the papillary layer which itself is more or less infiltrated. It is obvious that the tumor has invaded the skin from below upward. We shall study first the deeper portion of the tumor, corresponding to the hypoderm and the fibrous derma, then the superficial region beneath the epidermis.

### THE DEEPER REGION

*Low Power.*—After staining with trichrome (iron hæmatoxylin, ponceau and aniline blue), the tumor tissue is seen to be formed of pink bundles interlacing and anastomosing in all directions and incompletely separated by dark blue bands or septa of fibrous connective tissue. These bands represent the dermal or hypodermal connective



tissue; they are traversed by voluminous arteries which often run alongside of medullated nerve fibres. Embedded in the fibrous septa and often half fusing with the pink bundles there are rounded, oval or multilobular bodies formed of folded laminæ piled one on the other, obviously gigantic tactile corpuscles of the Wagner-Meissner type.

*High Power.*—(a) *The Bundles.*—At first sight, these bundles seem to be formed of elongated cells of purely but feebly acidophil protoplasm of homogeneous, glassy structure. In each of these cells there is an irregularly oval nucleus containing 2 to 3 karyosomes; each cell seems to be isolated from its fellows by a thin collagen sheath. More attentive examination shows that in reality these cells are not completely isolated but that their cytoplasm anastomose by prolongations sheathed with collagen. Each bundle, then, is formed of a multinucleated and plexiform syncytium. It has the same structure and the same significance as the *neuroid bundles* that I have described in *nævi*.



FIG. 3.—*Nævic* corpuscle of rounded form half-buried in a neuroid bundle of indistinct contour. On the right of this corpuscle, its constituents are seen to be continuous with the plexus formed by the cells of the neuroid bundle.

described elsewhere. This resemblance is all the more striking in that many of them become flattened and their cytoplasm is thus divided into thin, intercommunicating leaves by septa of reticulated collagen. These are typical leaflike laminæ.

(b) *The Nævic Corpuscles.*—These laminæ are rough sketches of tactile corpuscles. There are all intermediate forms between them and the gigantic tactile corpuscles illustrated in Figs. 1 and 2.

The corpuscles are always attached to the syncytium of the bundles. Sometimes they are half buried in a bundle (Fig. 3); sometimes they are distant and surrounded by connective tissue (Figs. 1 and 2) but connected with a neighboring bundle by a narrow pedicle, often laminated. It is obvious that they correspond to local differentiations of the cells of the bundles. The corpuscles never contain a nerve spiral; like the corpuscles of *nævi*, they consist solely of piled-up discs, laminated and intercommunicating, identical with those which form the supporting structure of normal Wagner-Meissner corpuscles.

If we now study the relation of these bundles to the medullated nerve fibres which

Silver impregnation by Laidlaw's method shows that the multiple collagenous sheaths of this plexus consist of a delicate network of reticulin, of which the most voluminous fibres run almost longitudinally in relation to the cell and are bound to one another by a transverse web of much more delicate fibres. This is exactly the disposition of reticulin around the medullated nerve fibres.

The border of the bundles is often well defined (Fig. 2, left); at other times indistinct (Figs. 2 and 3, right) because some of their cells escape more or less capriciously into the connective tissue. These aberrant cells may be very long, always surrounded by their sheath of reticulin; they are identical with the neuroid fibres or *nævi* that I have

traverse the connective tissue of the tumor and ramify there, we find the following situation. Most frequently the relations are distant; the nerves surrounded by their perineurium lie in the fibrous connective tissue separated from the bundles by a more or less thick layer of collagen fibres belonging to the derma or the hypoderm. Elsewhere, the nerves, still surrounded by their perineurium, are included in the tissue of the bundles but without continuity with them; or the tortuous nerve fibres, not surrounded by a perineurium, lose themselves among the cells of the bundle with which they seem to be continuous. This disappearance of the nerves in the bundles is not confined to any certain level but appears through the entire thickness of the deep zone. Furthermore, it does not involve all of the nerve fibres, many of which reach the superficial region of the derma, where we shall meet them presently.

By all of these characteristics, by its structure, by the tactile corpuscles to which it gives birth, by its relations with indisputable medullated nerves, the deep zone of our tumor must be considered as constituted of the Schwannian syncytium of the tactile nerves. It is a diffuse, fasciculated and plexiform neurinoma. Unfortunately the fixation of the tissue did not permit deciding if and in what measure neurites took part in its constitution.

The interesting observations of Itchikawa, then of Oertel, on the budding of nerves in the most diverse neoplasms, epitheliomas and sarcomas, and their invasion of tumor cells are well known. This phenomenon, the indisputable reality of which I have been able to confirm, by its generality lessens in great measure the importance that I formerly attributed to the presence of neurites in nævi as demonstrating their nervous nature.

*The Superficial Region.*—This region corresponds to the papillary layer and the upper half of the fibrous derma. Its aspect varies greatly at different points. In places the fibrous tissue is normal and free from all foreign cells; the tumor bundles have not extended above the deep region of the derma. At other points it is invaded more or less completely by the bundles, which change their aspect gradually as they approach the surface. In the neighborhood of the papillary layer, they lose little by little their coherence and the clearness of their contours. While remaining continuous, the syncytium enlarges its meshes, which become more and more conspicuous and insinuate themselves between the dermal fibres. Without any other modification, the tumor cells may thus gain the immediate vicinity of the epidermis. More often, however, when these superficial expansions of the tumor tissue reach the papillary layer, their cells lying nearest the epidermis change character gradually. Spherical or polygonal from reciprocal pressure, grouped in rounded masses or in columns, their character as epithelioid nævus cells is all the more obvious in that many of them contain melanin.

It should be noted that in the superficial region of the tumor there are no characteristic voluminous tactile corpuscles but merely the rough sketches, constituted by flattened or cylindrical neuroid fibres divided into imbricated or piled-up lamellæ by the collagen septa issuing from their sheaths. In all this region, many slender nerve filaments disappear among the tumor cells, with which they seem to be continuous.

Everywhere in the papillary layer there is a notable quantity of melanin, contained either in the fixed cells or in large macrophages ranged along the vessels. The pigment is distributed unequally; it is particularly abundant where there are masses of epithelioid nævus cells.

The epidermis presents similar pigmentary inequalities and, as in many other nævi, a few Langerhans' cells. At certain points, however, the Langerhans' cells have multiplied and accumulated (Fig. 4), forming more or less voluminous masses between the basal layer and the Malpighian cells. Nowhere do they seem to have migrated into the

derma or to have taken part in the formation of the nævus, contrary to that which, after Unna, so many observers, myself included, have seen in other nævi.

Thus constructed, our tumor possesses all of the histological features of a pigmented mole or, better, a neuro-nævus. By its extraordinary dimensions, it differs from those that I have described formerly. In this respect, it should be classed among the pachydermias of the hairy scalp first described



FIG. 4.—Superficial region of the neuro-nævus. Above, the epidermis, presenting a mass of Langerhans' cells which have proliferated at the tip of an epidermic ridge. All around it, the papillary layer contains fixed cells filled with melanin. On the right and below, many epithelioid nævus cells. These cells are continuous with the neuroid bundles of the deep zone, from which they seem to spring. In this specimen, none of the nævus cells seem to have migrated from the epidermis.

by Jadassohn and known as *cutis verticis gyrata* (Unna), *cutis verticis striata* (Veress), *pachydermie vorticillée* (Audry), the nævic nature of which was demonstrated by Malartic and Opin, Lenormant and Curtis. This specimen is a smooth pachydermia.

This tumor differs from ordinary nævi by the enormous development of the deep zone, which forms a vast fasciculated and plexiform neurinoma at least 1 centimetre thick, and by the gigantism of its tactile corpuscles.

It presents a further peculiarity, the inconstancy of the epithelioid cells which are found only at certain points in the superficial zone, often too distant from the epidermis to warrant an epidermal origin. This feature is of interest in showing that a nævus may be constituted in all of its fundamental characteristics without the epidermis playing any rôle whatever in its construction, all of its elements, even the superficial epithelioid cells, springing from the cutaneous nerves.

Since it is certain, in other specimens, that the Langerhans' cells migrate into the derma and are there transformed into epithelioid nævus cells and incorporated in the tactile neuroneurinoma growing up from the deeper zone, it is quite probable

that the normal Langerhans' cells are not of epithelial but of nervous origin.

# TRANSILLUMINATION OF THE BREAST

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TRANSILLUMINATION as a diagnostic aid in medicine has been largely confined to a very limited group of pathological conditions. Although this method has been employed for many years in the diagnosis of inflammatory conditions of the sinuses and in the differential diagnosis between cystic and solid tumors of the testis, its use in the breast before 1929 had been totally neglected. A careful review of the literature at that time failed to reveal any reports dealing directly with the use of transillumination in the differential diagnosis of breast tumors.

In June, 1929, the writer<sup>1</sup> reported the results of transillumination in a series of 176 breast lesions examined in the Memorial Hospital. Following this initial report the method was adopted in various American and European clinics. Since the writer's original communication, further observations have revealed some points of interest and practical importance in the use of this method. It is the purpose of this communication to relate briefly these newer observations, to state the conditions under which transillumination is an aid in the differential diagnosis of lesions in the breast and particularly to reemphasize some of the necessary precautions in the technic of examination and the interpretation of the findings.

When it is considered that a hydrocele transmits light readily and thus establishes the presence of clear fluid, it is at once obvious that a cyst of the breast containing clear fluid would transilluminate with equal facility. The importance of establishing the exact physical nature of a breast tumor is self-evident. For example, Bloodgood has demonstrated that a palpable cyst containing clear fluid is usually a benign lesion, whereas a cyst containing bloody fluid is, in the majority of instances, malignant. Sir Lenthal Cheatle<sup>2</sup> and Bloodgood agree that once a cyst becomes clinically palpable it may be regarded, with rare exceptions, as benign whereas the dangerous cysts are those of microscopic dimensions.

When a tense cyst is situated deep in the breast, it may be extremely difficult to detect its cystic character. Under these circumstances a deeply situated, benign cyst is usually regarded as a solid tumor and the radical operation is performed when only a local excision is necessary. This error is especially likely to occur when a superimposed inflammation gives rise to slight adherence of the overlying skin. The clinical picture of a firm tumor associated with skin adherence often leads to a diagnosis of carcinoma and the radical operation.

The conception that the transmission of light through tissue might yield information of practical value in diagnosis was first developed among the

members of the laboratory staff of the Memorial Hospital (New York) during the routine examination of breast specimens. The marked variations in the degree of translucence in different portions of normal and pathological tissues was especially impressive. These observations suggested the possibility of establishing some points of difference between tumors of different density. The problem of testing the translucence of various breast tumors instituted at the suggestion of Ewing was pursued by Adair,<sup>3</sup> who encountered difficulties because of the excessive heat developed by the transilluminating lamp.

It is important to appreciate that in common with other diagnostic methods, transillumination is an aid and not an absolute means of diagnosis. The method is based upon the varying translucence and opacity of different tissues. In the interpretation of the transillumination findings a knowledge of the underlying pathology of breast lesions is essential. Thorough familiarity with the gross anatomical and microscopical structure of lesions in the breast renders an interpretation of the transillumination findings more simple and leads to a more accurate judgment of the physical nature of the tumor. This information taken in conjunction with the clinical history and clinical findings enable differential diagnosis to be made with a greater degree of accuracy. With certain exceptions, transillumination alone has not enabled a differentiation between benign and malignant solid tumors nor can this accomplishment be expected. If the solid tumor is a hæmatoma this distinction is made without difficulty and the method constitutes the only non-operative means of establishing the diagnosis.

*Technic.*—Unless transillumination is performed in a totally dark room the result of the examination is not satisfactory. The transilluminating lamp must be a cold lamp of sufficient intensity to penetrate the tissues of the breast. It must be attached to a rheostat so that the intensity of the light can be varied conveniently by the examiner. The lamp must be so constructed as to permit the light to emanate from one point only in order that the light from this single source can be directed to the particular portion of the breast under consideration. The patient is placed in a sitting position and both breasts are examined routinely. The general scheme is to place the light directly beneath the lesion in question so that the part of the breast under consideration lies between the light and the examiner's eye. It is obvious that tumors that are attached to the chest wall are not amenable to transillumination. Under these circumstances the diagnosis is usually clear without the aid of this method. In tumors situated deeply in a thin, flat breast it may be more convenient to transilluminate from side to side.

It is necessary to emphasize that careful attention to the intensity of the light is a most important detail in the technic. The most formidable source of error is the over-illumination of small solid tumors thus establishing a false translucence. This error usually occurs when the tumor is small and especially when because of its superficial situation in a thin, flat breast the strong

light is placed in close proximity to a small mass. Under these circumstances the light diffuses around the tumor and a shadow cannot be detected. If the lamp is held in place and the intensity of the light reduced by means of the rheostat, a shadow will be noted which is faint at first but increases as the intensity of the light is diminished. It is highly important, therefore, when examining small lesions to reduce the intensity of the light to a minimum and to interpret the faintest shadow as positive. This important detail was pointed out in the original description of the method and was subsequently reëmphasized when it was learned that this source of fallacy had not been sufficiently stressed.<sup>4</sup>

Fat is highly translucent, consequently the large fat breasts transilluminate very satisfactorily. Dilated ducts and acini filled with epithelial débris and stagnant secretions are opaque to transillumination. Breasts in which this process is pronounced fail to transmit light readily. Breasts which are the seat of Schimmelbusch disease may fail to transmit light of the intensity usually employed.\* The satisfactory transillumination of these breasts requires a light of greater intensity.

The technic of transillumination of the breast is relatively simple. The patient is examined while sitting on a revolving chair. The lamp is held against the under surface of the breast and gradually moved as different areas in the breast are inspected successively; the object being to place the particular site in question directly between the light and the examiner's eye. By means of gentle pressure on the upper surface, thus compressing the organ between the hand above and the light beneath, the degree of translucence may be increased. The tail of the breast is best transilluminated by placing the small curved lamp underneath the axillary fold, and directing the light anteriorly.

*The Normal Breast.*—Marked anatomical and physiological variations in normal breasts are well recognized. The appearance of the normal transilluminated breast depends upon its anatomical structure which in turn depends, to some extent, upon its physiological state.

The wide variation in the anatomical constituents of the normal breast is paralleled by corresponding differences in the degree of translucence. Fat is highly translucent; fibrous tissue is less translucent. Solid epithelial masses, fibro-epithelial masses, and epithelial débris are moderately opaque and blood is intensely opaque. Fat breasts transilluminate well regardless of their size. As the fibrous and epithelial contents of the breast increase, the degree of translucence diminishes.

A breast which is the seat of mazoplasia (chronic mastitis) is less translucent than a perfectly normal breast. The diffuse opacity is more marked before and during the menstrual periods when the hyperplasia of the duct

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\* The author is grateful to the General Electric Company for its aid and coöperation in developing a more intense light, and to Doctor Failla for his help in constructing a special lamp suitable for transillumination in these cases.

and acinous epithelium is most pronounced. Dilated ducts and acini filled with desquamated epithelial debris are barriers to the passage of light; consequently parts of the breast in which the hyperplastic process is most marked show corresponding relative opacities.

It is important to point out that small, flat, non-pendulous breasts closely applied against the chest wall are unsuitable for transillumination. Lesions situated in the depth of this type of breast cannot be transilluminated satis-



FIG. 1.—Appearance of the normal breast on transillumination.

factorily as it is practically impossible to place the lesion between the lamp and the examiner's eye. Superficial lesions, however, can be examined quite satisfactorily by transilluminating with a small lamp from side to side.

*Cystic Tumors.*—Cysts containing clear fluid are translucent. This finding renders transillumination a valuable aid in the interpretation of the physical nature of tumors in the breast in which clinical examination leaves a doubt as to the solid or cystic nature of a mass.

The absolute knowledge of the precise physical nature of a breast tumor is usually of considerable prognostic diagnostic and therapeutic importance. In many instances, clinical examination alone yields sufficient information to establish the diagnosis. That errors in differential diagnosis in this field occur with marked frequency is well known to all who have examined a considerable number of breast tumors and followed them to operation. An

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early and very cellular carcinoma may present a circumscribed elastic tumor that gives many of the physical signs of a benign cyst. The true nature of the lesion is discovered only after local excision and section of the tumor. Deep-seated cysts distended with fluid fail to give fluctuation on palpation and present many of the clinical signs of carcinoma. This error is most likely to occur when the superimposition of an inflammatory process causes slight adherence of the mass to the overlying skin. Under these circumstances a simple benign cyst gives the impression of a firm solid tumor and in the presence of skin adherence, the logical diagnosis of carcinoma is made.

A knowledge of the nature of the cyst contents may be of considerable help. A clinically palpable cyst filled with clear fluid usually signifies a benign lesion. If the cyst contains blood there is strong evidence of intracystic papilloma or duct carcinoma. The opacity of blood is intense and transillumination enables a differential diagnosis between a cyst containing clear fluid and one containing blood.



FIG. 2.—Opacity on transillumination of a solid tumor in the breast.

Solid tumors are opaque to transillumination. The opacity corresponds to the extent of the mass. The character of the opacity differs from that caused by the presence of blood in being much less intense. Thus transillumination enables a differential diagnosis between cysts filled with blood and solid tumors (carcinoma or fibro-adenoma).

*Lactation—Galactocoele.*—The lactating breast is totally opaque to transillumination. The opacity of milk is also demonstrated by the appearance of a galactocoele on transillumination. The tumor presents a sharply circumscribed and opaque shadow. Since the differential diagnosis of galactocoele



from other lesions in the breast is usually not difficult clinically, the practical application of this finding is of limited value. In certain cases, however, in which the clinical diagnosis is otherwise in doubt, transillumination may prove to be of considerable help in interpreting the precise nature of the lesion.

*Hæmatoma.*—The intense opacity of blood to transillumination has been pointed out. In view of this observation it was expected that hæmatoma of the breast following injury might present a special appearance on transillumination. The frequency with which a history of trauma is volunteered by the patient as a cause of lumps in the breast is well known. Since the breast is an organ subject to frequent and repeated trauma, the correct evaluation of such information is exceedingly difficult. The peculiar tendency of the

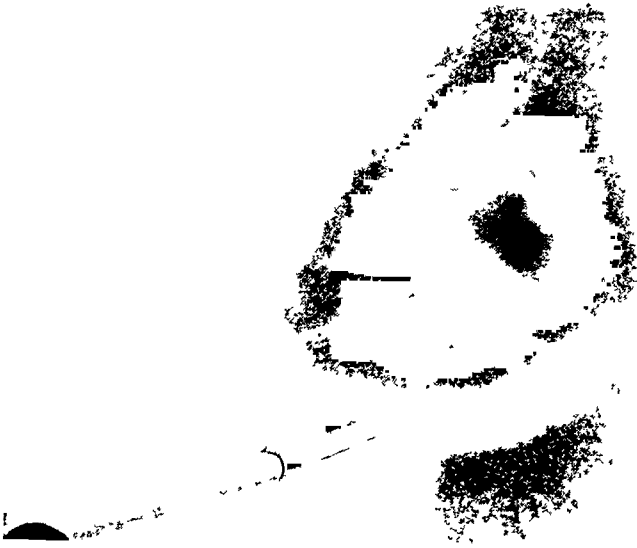


FIG. 3.—The appearance of a hæmatoma on transillumination. The opacity is intense, uneven and irregular in outline.

patient to attribute a lump to a specific cause, and more particularly to trauma, is well known and upon careful questioning the fact is often elicited that no relationship exists between the trauma and the tumor. On the other hand, a direct and inseparable causative relationship between trauma and tumor formation cannot be escaped in certain cases even on the closest critical analysis.

In some cases a definite trauma to the breast is soon followed by the appearance of a discrete tumor. Discoloration of the skin may or may not have been noticed by the patient. In these cases a differential diagnosis between hæmatoma and beginning carcinoma is exceedingly difficult, yet most important from a therapeutic standpoint. Frequently, slight skin adherence complicates the clinical picture and renders a diagnosis still more difficult.

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Transillumination has been found to be of considerable aid in the differential diagnosis under these conditions. The opacity of a hæmatoma, being due to unabsorbed blood, is intense. The opacity varies in degree according to differences in the amount of unabsorbed blood pigments in various portions of the lesion. The edges are irregular in outline and extend into the surrounding breast tissue beyond the palpable edge of the tumor. This irregular edge is due to the extravasation of blood into the surrounding tissues.

When the lesion is examined at repeated and frequent intervals after the injury it is noted that the opacity slowly diminishes in extent and intensity and finally completely disappears. In several cases three months elapsed before the final and total disappearance of the opacity. The diminution in the extent and intensity of the opacity is accompanied by a corresponding decrease in size of the tumor.

These transillumination findings may be readily correlated with the changes known to occur in the various stages of hæmatoma formation and absorption, remembering that the opacity is due to the unabsorbed blood pigments. The opacity found in this state is unlike that seen in any other condition. It differs from that caused by an intracystic papilloma in that the latter produces a circumscribed uniform shadow with sharply defined edges. It differs from the opacity of a solid tumor such as carcinoma, in its intensity, which is never equalled by any lesion in which blood pigments do not participate.

In cases of this type, in which a differential diagnosis between hæmatoma and beginning carcinoma must be made at once, transillumination may be the means of preventing an unnecessary mastectomy. In several cases the breast was saved because of these findings. If the characteristic shadow of hæmatoma is discovered by transillumination, it is safe to withhold operation and examine the breast at frequent intervals. The slightest diminution in size of the mass accompanied by a decrease in the extent and intensity of the opacity is an indication that a hæmatoma exists and is undergoing absorption. Under observation the entire mass may disappear and an unnecessary operation is thereby avoided.

*Transillumination of the Breast in the Presence of a Hæmorrhagic Discharge from the Nipple.*—In order to interpret correctly the transillumination findings in this group of cases it is important to refer briefly to the pathological anatomy underlying this syndrome. Although numerous important researches have been conducted in this field it is a remarkable fact that the significance of a hæmorrhagic discharge from the nipple still remains a matter of dispute among clinicians and pathologists. Some investigators hold that a hæmorrhagic discharge from the nipple of a non-lactating breast is evidence of a benign rather than a malignant lesion and is an almost positive sign of intracanalicular papilloma. (Bloodgood,<sup>5</sup> Greenough and Simmons,<sup>6</sup> Deaver and McFarland,<sup>7</sup> Sistrunk<sup>8</sup>) Miller and Lewis,<sup>9</sup> on the other hand, found the same proportion of benign and malignant tumors associated with

this sign and Judd,<sup>10</sup> in a review of one hundred cases, reached a similar conclusion.

Studies of whole sections of the mammary gland in cases of bleeding nipple have yielded important information concerning the underlying pathological process. By this method Sir Lenthal Cheate<sup>11</sup> has demonstrated that papillomata are more often multiple than is generally supposed. The uniradicular type of papilloma, usually multiple, occurs in the deeper portions of the breast and is rarely malignant. The multi-radicular type, usually occurring singly, and situated near the ampulla of the ducts, is more likely to undergo malignant changes. In a study of a large series of breasts associated with bleeding from the nipple, Knoflach and Urban<sup>12</sup> found that the common lesion is a circumscribed, mostly single, occasionally multiple, papillary growth in ducts or acini, showing the histological features of a benign process. Adair,<sup>3</sup> on the other hand, in a recent and very comprehensive study of an extensive series of cases of bleeding nipple, found that 50 per cent. of the lesions were malignant.

Careful palpation of a breast which is the seat of bleeding from the nipple sometimes reveals a tumor or a localized nodularity. In most cases, however, palpation of the breast fails to show a localized tumor and if an indefinite tumor or nodularity is discovered it may not constitute the lesion which causes the bleeding. In the absence of a localized tumor, point pressure in the region of the areola may help in localizing the lesion but this test often fails.

Owing to educational propaganda within the last few years, women now come for examination soon after a hæmorrhagic discharge from the nipple is detected. Consequently the proportion of cases in which a hæmorrhagic discharge from the nipple is unaccompanied by the presence of a palpable tumor, is constantly on the increase. Within the last few years the majority of such cases have applied for treatment so soon after observing this sign that no palpable evidence of the disease existed when the breast was first examined.

The inability to localize the lesion in cases of bleeding from the nipple is extremely embarrassing, from a therapeutic standpoint. Those who look upon this sign as of serious import, practice the removal of the entire breast. This is certainly the safest procedure but in view of the fact that the underlying lesion is often a simple benign papilloma, a removal of the entire breast may be unnecessary in many cases. Bloodgood reports two cases in which the breast was removed and small benign papillomatous cysts containing blood were found when the breasts were sectioned. Miller and Lewis<sup>9</sup> state that when a serohæmorrhagic discharge occurs and no tumor is palpable, the lesion is, in all probability, a small benign intracanalicular papilloma situated deep in the substance of the breast and should be removed locally. Knoflach and Urban<sup>12</sup> comment on this group of cases and point out the difficulties in localizing the lesion. They state that in many cases it is not possible to locate a point at which pressure causes bleeding from the nipple even after repeated

examinations. Thus it is obvious that any procedure which enables an accurate localization of the lesion and a better conception of the distribution of the disease throughout the breast would be of considerable help in the treatment of these cases.

The intense opacity of blood has been pointed out. The most striking feature of the transillumination of the normal breast is the prominence of the blood vessels. In view of these findings it was logical to expect that an intracystic papilloma associated with bleeding would yield an opaque shadow on transillumination. This suspicion was readily confirmed when the first breast was examined by this method. It soon became evident that this simple procedure constituted an invaluable aid in the localization of the small intracystic papillomata associated with bleeding from the nipple.

An intracystic papilloma which is accompanied by a hæmorrhagic discharge from the nipple presents a discrete and well circumscribed opacity that is characterized by two features: (1) its intensity; and (2) its sharply outlined periphery. In some examples, not only has the papilloma itself been localized, but the duct filled with blood leading to the surface of the nipple, could be readily followed throughout its course.

It is important to emphasize in this connection that minute papillomata may fail to cast a shadow. It is very important, when attempting to localize these small lesions, to reduce the intensity of the light to a minimum. The most common error that is made and one that leads to a failure to localize the small lesions is over-illumination. This error is especially likely to occur when the small lesion is situated close to the surface of the breast.

If a local excision is to be performed, it is important to mark the skin directly overlying the opacity with indelible ink or with silver nitrate. This procedure must be carried out while the patient is lying in the same position in which she is to lie when the tumor is to be excised. These precautions greatly facilitate the surgical procedure. In rare cases, neither palpation nor transillumination reveals the site of the lesion. In two such examples the lesion proved to be very early duct carcinomata. No tumor could be felt on palpation and the transillumination findings were negative. Both lesions were of microscopical dimensions.

*Multiple Papillomata.*—Whereas in most cases a hæmorrhagic discharge from the nipple is caused by a single localized and circumscribed lesion, the underlying cause in some cases consists of a diffuse pathological process with numerous minute papillomata in dilated ducts. Although the association of multiple papillomata with a hæmorrhagic discharge from the nipple has been previously recognized, a clinical differentiation of these cases from those in which a single lesion is the causative factor has not heretofore been possible. This group of cases presents an important therapeutic problem. Knoflach and Urban<sup>12</sup> advise a complete mastectomy in this group as against a local excision in the other group. Their procedure consists in local excision of the suspected area, and, if the microscopic examination of the excised specimen indicates a diffuse process, a second operation is performed and the

entire breast is removed. This double procedure is necessitated by the inability to differentiate clinically between cases of single and multiple lesions. These authors report three cases in which local excision alone failed to stop the bleeding from the nipple, one case requiring a second operation. They warn against a too narrow excision because of the danger of leaving pathological tissue in the breast. Transillumination of the breast in these cases presents a striking picture consisting of multiple small opacities throughout the affected breast and sometimes also in the opposite breast. The opacities are intense, discrete, and localized. Adair<sup>3</sup> has found transillumination a valuable aid in the diagnosis and treatment of this group of cases.



FIG 4—Multiple opacities seen on transillumination of a breast containing several papillomata

It is important to emphasize that when the discharge from the nipple is not distinctly hæmorrhagic, localization by transillumination is often impossible.

#### SUMMARY AND CONCLUSIONS

1 Transillumination is a practical aid in the differential diagnosis of pathological conditions in the breast.

2 Different tissues display varying degrees of translucence. Fat is highly translucent. Fibrous tissue is less so. Epithelial and fibro-epithelial masses are opaque and blood is intensely opaque.

3. Transillumination enables a more accurate estimate of the physical nature of a tumor than can be gained by inspection and palpation alone. This

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information, correlated with a careful history and with the physical findings enable a more accurate judgment of the underlying pathological process than can be gained without the use of this method.

4. The normal breast presents marked variations on transillumination depending upon the relative content of fat, fibrous tissue and epithelial elements.

5. Three important technical details, to a large extent, determine the success or failure of this method. (1) The room in which the examination is performed must be totally dark. (2) When examining small lesions the intensity of the light must be reduced and the faintest shadow must be interpreted as positive. (3) In examining certain breast lesions (Schimmelbusch disease) the intensity of the light must be markedly increased.

6. Solid tumors are opaque to transillumination. The opacity lacks the intensity of the shadow cast by blood. The character of the opacity in itself does not permit of a differentiation between benign and malignant tumors.

7. Cysts containing clear fluid are translucent. This finding may be of considerable aid in differentiating between carcinoma and tense, deeply seated cysts which present the clinical features of solid masses.

8. The intense opacity of blood is one of the most characteristic and important findings in the transillumination of different tissues.

9. Traumatic hæmatoma presents a specific and characteristic appearance on transillumination. The opacity is intense, uneven and irregular in outline. When the lesion is examined at repeated intervals the opacity diminishes in its extent and intensity and finally disappears as the blood pigments are absorbed. This finding may be of considerable importance in differentiating this lesion from carcinoma especially when traumatic hæmatoma is accompanied by skin adherence.

10. Intracystic and duct papilloma associated with a hæmorrhagic discharge from the nipple, present a characteristic appearance on transillumination. The opacity is intense, uniform and sharply circumscribed.

11. Transillumination is especially helpful in cases presenting a hæmorrhagic discharge from the nipple in which no tumor can be palpated in the underlying breast. In this group of cases transillumination may constitute the only available method of localizing the lesion and indicating the site for surgical removal.

12. A hæmorrhagic discharge from the nipple may be associated with a single papilloma or with multiple papillomata. Multiple papillomata (with the exception of microscopical lesions) present multiple opacities. Transillumination is therefore of considerable aid in determining the extent of the disease in the underlying breast and constitutes the only non-operative means of differentiating between single or multiple lesions. This determination is of special importance from a therapeutic standpoint in indicating the extent of the surgical procedure.

13. The practical importance of differentiating between single and multiple papillomata is emphasized by those examples in which the local removal

of a duct papilloma has been followed by further bleeding from the nipple. Subsequent transillumination in these cases has revealed the fact that only one of numerous papillomata had been removed.

14. Transillumination is a simple procedure and a valuable aid in the interpretation of pathological conditions in the mammary gland. Its use is recommended in the routine examination of the breast.

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## BORDER-LINE BREAST TUMORS\*

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THIS term seems to have been employed to define a lesion of the breast difficult to diagnose either clinically, or from its gross appearance, or from repeated microscopic studies, by a number of pathologists. In the great majority of cases the first diagnosis by the majority of the examiners has been malignant, yet the follow-up demonstrated that the lesion was benign.

These border-line tumors can be classified first into four main groups: (1) Clinically malignant, microscopically benign. (2) Gross picture malignant, microscopic picture benign. (3) Gross picture benign, microscopic picture malignant. (4) The largest group. Here, in the first instance, the first microscopic diagnosis was malignant. When the section is submitted to a number of pathologists, the majority favor the diagnosis of malignancy, but subsequent events and restudy all prove that the lesion is benign.

These border-line tumors of the breast were very rare between 1890 and 1900, because the majority of women with lumps in the breasts delayed one year or more. In this period the majority of examples of chronic cystic mastitis spontaneously disappeared, as did some examples of galactocoele, chronic lactation mastitis, and traumatic mastitis. Malignant tumors assumed not only the clinical picture of malignancy, but the positive microscopic characteristics of fully developed carcinoma of various types. In each decade, as the duration of the lump observed by the patient grows less, the relative frequency of the border-line tumor increases. But there are other factors, and Velpeau called attention to this in the second edition of his book on tumors of the breast. In the first edition all the diagnoses by Velpeau were based upon the clinical picture and the gross appearance. The microscope was employed more and more frequently after the publication of the first edition. In the second edition of his book this great French surgical pathologist stated that the microscope has been of little or no value to him, because the pathologist looking through the microscope diagnosed cancer when Velpeau was confident, from his vast clinical and gross experience, that the lesion was not cancer; and diagnosed benign when he was certain that the lesion was malignant. Velpeau did not live to learn the value of cellular pathology as discovered by Virchow, not to know how to explain the different interpretations between his own and this pioneer group of microscopic pathologists. More than sixty years later Welch, in making a tour of the United States, observed the same differences of opinion between the surgeon of large experience and training in the clinical and naked-eye diagnosis of tumors, and the young and inexperienced pathologists but recently called upon to diagnose



with the microscope material fresh from the operating room, either from immediate frozen sections or later permanent sections. (Professor William H. Welch, of the Pathological Department of Johns Hopkins University, confirmed Velpeau's statement made in about 1850.) The pathologist was usually incorrect. But when a pathologist of Welch's experience in the microscopic diagnosis of tumors and a surgeon of an equal experience, as William S. Halsted, conferred on a breast tumor, the clinical and naked-eye diagnosis of Halsted usually agreed with the microscopic diagnosis of Welch. Our records show that in every clinic, when the material from the operating room was sent to the pathological department and this department was not in the hands of specially trained pathologists, there was a great difference of opinion between the diagnosis of the operator and the microscopic diagnosis of the pathological department. This factor, therefore, influences the relative number of border-line cases.

I shall describe here a typical border-line case of breast tumor which was reported in Halsted's first article on the results of his operation for cancer of the breast in 1895, as cancer of the breast cured by operation. We are now convinced that this case was a chronic lactation mastitis abscess. The patient is living and free from disease today.



FIG. 1.—Case I. Pathol. No. 228. Section of wall of chronic lactation mastitis abscess. Diagnosed cancer in 1894. Complete operation. The patient is well, no recurrence today. See text page 236.

visible. I took the history, made the examination and assisted Dr. J. M. T. Finney at the operation.

Neither Doctor Finney nor myself at that time had had much experience with tumors of the breast. We both thought it was an abscess. In cutting down upon it to drain it we passed through normal skin and fat; then a zone of breast tissue from which milk flowed, and then a zone of breast tissue that looked different from the first zone and from the surface of which no milk exuded; then came a very thin zone like granulation tissue. The material filling the cavity did not resemble pyogenic pus, still called laudable pus in those days; it was very much thinner, resembling the thinnest kind of skimmed milk. It is quite possible it was milk and not pus. But no examinations were made, unfortunately, either chemical, bacteriologic or microscopic, of this fluid. On the other hand, it did not have the appearance of the so-called cold tubercular abscess. The character of the fluid made such an impression upon us that that Doctor Finney excised the wall of this cavity and closed the wound. Within a few days Doctor Welch examined the sections (Fig. 1) and was inclined to the diagnosis of adenocarcinoma in a lactating breast. Doctor Halsted agreed with this microscopic diagnosis and performed the complete operation for cancer. The glands in the axilla were not involved. Some three

## BORDER-LINE BREAST TUMORS.

years later a nodule like a skin metastasis developed on the arm. This was excised and found to be microscopically a fibroma. The patient had a number of children after this operation; nursed them without difficulty. She was followed for more than twenty-five years. This section was one of a number which I submitted in 1915 to a group of the most experienced and trained pathologists in this country. At that date the majority diagnosed cancer or "suspicious of cancer," or adenocarcinoma.

This is the best example of a border-line breast tumor, and allows us to give the evidence which justifies the conclusion that the microscopic diagnosis in the original was incorrect, and that this patient's breast could have been saved. Today, properly trained surgical pathologists would be able to recognize at the biopsy at exploratory incision, the distinct benignancy of the lesion, because clinically and even in the gross, the picture was unusual. In the first place, cancer cysts during lactation are possible. The history of the cancer cyst would undoubtedly be identical with this chronic lactation abscess



FIG. 2.—Case II. Pathol. No. 1734. Non-encapsulated cystic adenoma. Largely solid large-duct adenoma. Diagnosed cancer at Johns Hopkins in 1897. The patient lived sixteen years without recurrence. See text page 242.



FIG. 3.—Case III. Pathol. No. 26650. Section from wall of blue-domed cyst; large, solid duct-adenoma resembling Fig. 2. Diagnosed by Bloodgood at St. Agnes Hospital, benign. Cyst removed. No recurrence in 1930. See text page 243.

or galactoceles. Both would be slowly growing, more or less painless tumors. Both would give fluctuation on palpation. In both instances there would necessarily be no change in the production of milk. Up to the present time, in my experience, the contents of a cancer cyst have either been bloody, or thick, grumous material. On one occasion it was smoky. Never have we recorded pus of the pyogenic or tubercular type, or milk-like contents. In one instance the contents of the cancer cyst has been smoky, and the operator made the diagnosis of a benign cyst and neglected the check of a frozen section. But the section of every cancer cyst recorded in the laboratory is typical of cancer and entirely different from the section of Pathol. No. 228. (Fig. 1.)

As a positive proof that Pathol. No. 228 is chronic inflammation in a lactating breast and not cancer, we have sections from a few cases of typical, clinically, lactation mastitis abscess. The surgeon in the operating room

incised the abscess and for the first time excised a piece of its wall, because there had just been introduced in his hospital a pathological department for the microscopic study of tissues removed in the operating room. He sent this tissue to the laboratory not because he wished it diagnosed, but because he wanted to obey the new rule of the hospital. To his surprise, in a few days he was informed that it was a cancer cyst, that the sections of the wall of this abscess showed undoubted cancer. As these operators were older surgeons of accumulated clinical experience in naked-eye diagnosis, they refused to accept this diagnosis and submitted the sections to a number of more experienced microscopic pathologists. They finally accepted the diagnosis of the minority group, of benign chronic lactation mastitis. These patients have been followed for years. None have developed malignancy in this or the other breast. In the past ten years no such example of an



FIG. 4.—Case IV. Pathol. No. 42770. Section of non-encapsulated solid and cystic area of breast. (Doctor Cullen's case.) This area suggests benign solid adenoma and papillary cystadenoma. For more suspicious areas in the same case, see Figs. 5 and 6.

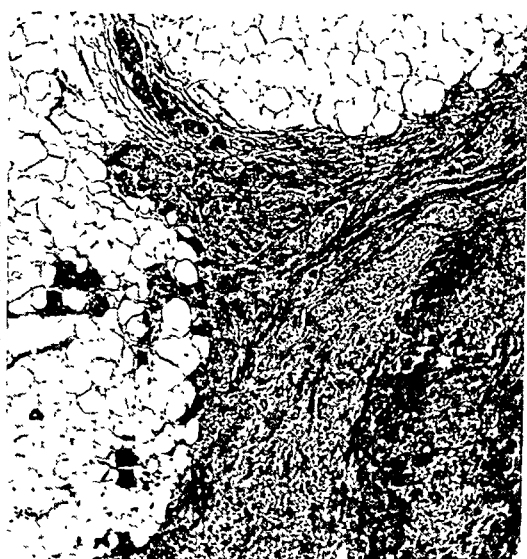


FIG. 5.—Case IV. Pathol. No. 42770. Low-power photomicrograph from solid area near Fig. 4. Suggests cancer. For high-power see Fig. 6.

abscess in a lactating breast has been diagnosed clinically or in the gross, or from a section, to be malignant. I am inclined to think that this group, in which there is a definite abscess in the chronic lactation mastitis, will give no further trouble. Nevertheless, we must teach this to our students, surgeons must bear it in mind, and pathologists assuming the responsibility of frozen-section diagnosis in the operating room must remember that in the past some experienced pathologists have made the mistake of seeing cancer in the wall of an abscess in a lactating breast. As these abscesses are becoming very rare, because we now know how to instruct the nursing mother to keep the nipple clean and free from infection, one may appear suddenly in any clinic, the operator may not know that an abscess in a tumor of the breast excludes cancer, and the pathologist may not have seen the remarkable epithelial changes in lactating breasts the seat of inflammation, acute or chronic.

*Chronic Lactation Mastitis Without Pus Formation, with the Gross and Microscopic Appearance of Cancer.*—My associate, Dr. L. Clarence Cohn, will soon publish his recent studies of this group. He finds twenty examples in more than 75 per cent. of which the benign inflammatory tumor has been diagnosed cancer either because, clinically, there was retraction of the nipple or dimpling of the skin, or because it had the naked-eye appearance of cancer at exploration, or because the frozen or the permanent section was difficult to distinguish from cancer. These cases are found in the records from the earliest years to the most recent months. If the sections of these twenty tumors are studied, you will find a microscopic picture much more difficult to differentiate from cancer than the sections of the fully developed abscess wall. In spite of the fact that these inflammatory lesions of the lactating breast are growing relatively less frequent, we should teach our students and the operating surgeons and the pathologists throughout the country the importance of this group and the necessity of preparation for this diagnosis. I shall refer constantly to this point. When the incidence of cancer dropped from 80 per cent. to 17 per cent. in the entire group, and the actual proportion of malignant tumors at operation has fallen from 80 to 50 per cent., the necessity of microscopic diagnosis from frozen sections increases, and the number of tumors difficult to recognize even

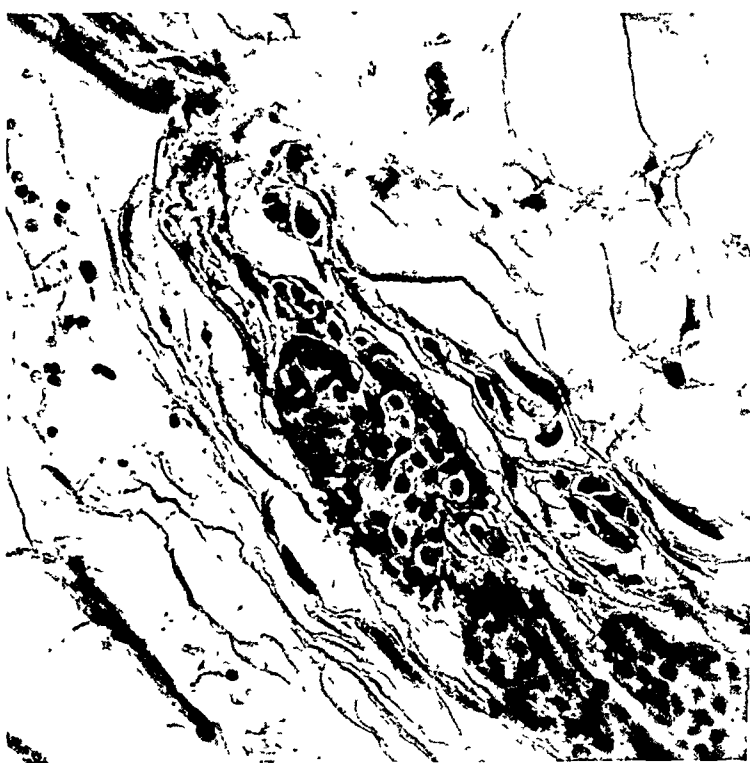


FIG. 6.—Case IV. Pathol. No. 42770. High-power area shown in Fig. 5. See text pages 247 and 248.

with the microscope increases. Every pathologist responsible for the frozen-section diagnosis in the operating room should constantly restudy sections of chronic lactation mastitis which have been verified as benign and all his other border-line tumors. The object of this paper is to bring this about.

Chronic lactation mastitis, like tubercular mastitis, and even traumatic mastitis, begins as an area of induration in some part of the breast. The size varies with the duration of the lesion; it is usually a single lesion and not bilateral. The area does not palpate at all differently from an area of scirrhus carcinoma, and there is a type of cancer of the breast that, clinically, is practically identical with mastitis. Therefore the differential diagnosis must be made at biopsy.

After writing up to this point and having before me the great mass of material of this group of border-line tumors, I find it impossible within the space assigned to me to cover the ground in the systematic manner I hoped to do. This must be left to a later monograph.

I am, therefore, taking the liberty of making this paper an introduction to the monograph. The entire staff of the Surgical Pathological Laboratory

have taken up the subject of breast tumors, and I hope this investigation will be finished, so that the most important conclusions can be summarized in the final word on border-line tumors. At the present moment I have the evidence to show that family physicians, surgeons and pathologists throughout this country, in every locality in which women are learning the correct facts in regard to breast lesions, are encountering more difficulty in the increasing number of patients who seek an examination for pain, discharge from the nipple, slight irritation of the nipple, and an indefinite lump. When the incidence of cancer is 17 per cent. and the operative group of definite tumors 35 per cent., of which more than one-half prove to be benign, and the group



FIG 7.—Case V. Pathol No 42546. Photograph of gross specimen showing cystic and solid areas in a nonencapsulated palpable tumor in the breast, clinically benign. For photomicrographs of this see Figs 8, 9 and 10.

which should not be operated upon 65 per cent. or more, the difficulties of distinguishing the benign condition for which operation is not indicated reach their height.

The second and perhaps greater dilemma is when this early tumor is explored. Definite benign lesions, instead of being 20 per cent. as they were twenty-five years ago, have increased to 50 per cent., and there is an increasing

number of non-encapsulated tumors of various types that are difficult to distinguish from cancer even in the frozen section.

In examining the breast, we run a greater risk of overlooking malignant disease in its earliest and most curable stage. At the operation we have to decide so frequently between the danger of an incomplete operation for cancer and the unnecessary mutilation of removal of the breast for innocent lesions.

What is the evidence to justify the conclusion that the majority of these border-line tumors are benign even when the major opinion of the pathologists to whom the sections have been referred is that it is malignant? If we take the border-line tumors recorded in every group, whether benign or malignant, and place them together, we will observe that the only evidence of cancer is an occasional cancer in the one breast left behind, or in the breast from which the border-line tumor has been removed, and the per cent. of such instances is not more than the risk of cancer incurred by any woman of



FIG. 8.—Case V. Pathol. No. 42546. Benign cystic-adenomatous area near the wall of the cyst shown in Fig. 7.

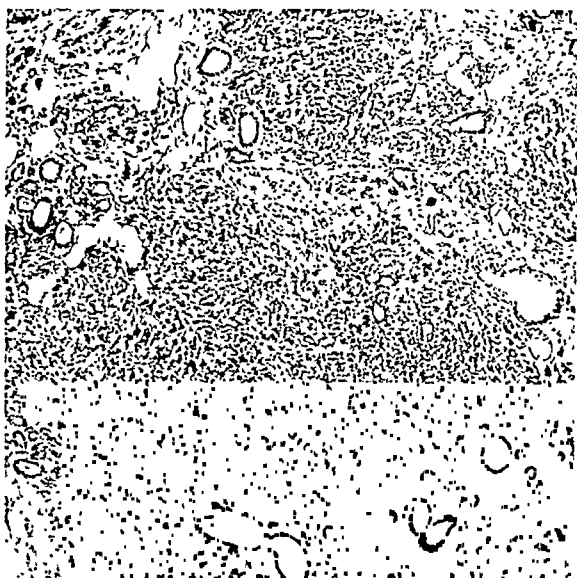


FIG. 9.—Case V. Pathol. No. 42546. Low-power solid area some distance from the cyst shown in Fig. 7, having gross appearance of cancer. See Fig. 10.

equal age over the same period of time. In none of the border-line tumors have the glands shown metastasis. In 1915, when the border-line tumors were separated from the malignant group, the per cent. of five-year cures after the complete operation for cancer in which the axillary glands, microscopically, showed no metastasis, dropped from 85 per cent. to 70 per cent.

This border-line group has always exaggerated the operative cures of cancer of the breast, and this is encouraging many surgeons in recent years to use radiation of the breast after biopsy.

The border-line tumors have given the evidence that it is not dangerous to excise a breast tumor, refer it to a pathologist for microscopic diagnosis, and then, some weeks or months later, to perform the complete operation for cancer.

It seems best now to give a few specially selected cases with illustrations,

with few exceptions, including the microscopic pictures. Only those in which the interval after operation is five years or more will be included.

CASE II.—(Fig. 2.) Observed in 1897. Pathol. No. 1734. In 1897 Doctor Halsted explored this distinctly palpable tumor in a woman aged forty-six, in which the small tumor beneath the right nipple had been present two years. There were no clinical signs of cancer. At the exploration the tumor was a non-encapsulated area containing a few cysts, a few dilated ducts from which could be expressed milk and brownish fluid, although there had been no discharge from the nipple. It is to be remembered that Halsted was a remarkable surgical pathologist. The tumor did not impress him as cancer, and a frozen section which was rarely made at that date was interpreted as benign. Later, after a careful study of the permanent sections, the diagnosis of adenocarcinoma was made and the complete operation was performed. This patient was followed for sixteen years to the age of sixty-two, and the letter addressed to the patient was returned marked "lost." Her physician wrote to me that he had lost track of the patient.

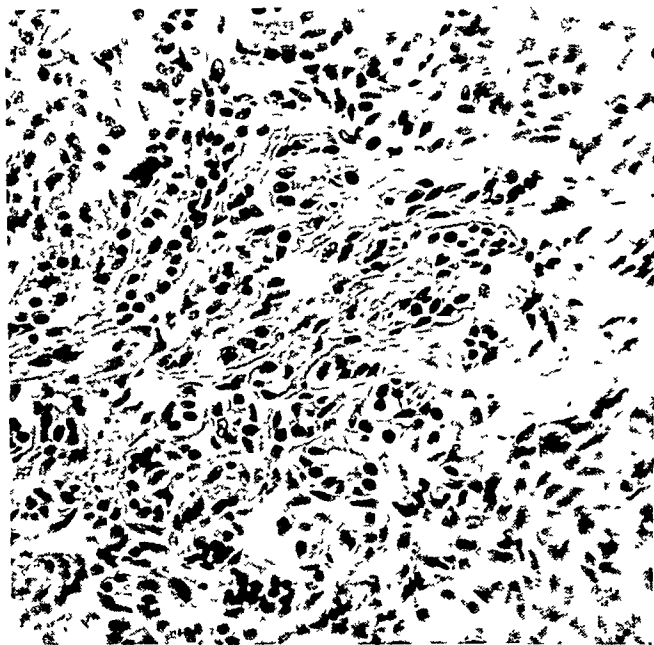


FIG. 10.—Case V. Pathol. No. 42546. High power of area shown in Fig. 9, interpreted by the operator, Doctor Cohn, as cancer. Complete operation performed. Glands not involved. Pathologists disagree.

This observation was almost unique among the group of tumors in Halsted's clinic previous to 1900. Remember, the tumor had been present two years and was still clinically benign, which is always, even today, evidence in favor of benignancy. Between 1897 and 1921, twenty-four years, we recorded in the laboratory eighteen examples of non-encapsulated cystic adenoma similar to this case illustrated in Fig. 2. All of them were ultimately subjected to the complete operation for cancer. In none of the cases were the glands involved; not one has died of cancer. I have reported them in the *Archives of Surgery* in November, 1921. When the section shown in Fig. 1 was submitted to pathologists in many cities in 1915, in over 60 per cent. the diagnosis was *adenocarcinoma*, and all advised the complete operation for cancer. In spite of this there is not a single example in our laboratory of a tumor of the breast in which the glands were involved, or one in which the patient has ultimately died of cancer, with a microscopic appearance resembling Pathol. No. 1734.\* (Fig. 2.) As this section is given out in the examinations students find great difficulty in distinguishing it from cancer of the comedo-adenocarcinoma type. It is our best example,

\* Fig. 60, page 503, in the *Archives of Surgery*, *loc. cit.*

## BORDER-LINE BREAST TUMORS

during these forty years, of a border-line tumor. The more familiar one is with the varying microscopic pictures of chronic cystic mastitis, the less difficult it is to recognize malignancy. But this picture, which is not unlike that seen in a lactating adenoma, is rare in any example of chronic cystic mastitis. It is not a common finding in the breast tissue surrounding a blue-domed cyst. (See Fig. 3, Pathol. 26650.)

### CASE III.—(Fig. 3.)

Observed in 1920. Pathol No. 26650. This photomicrograph of an area of chronic cystic mastitis is taken from the wall of a blue-domed cyst removed in 1920, ten years ago. The patient has had no recurrence in either breast since then, in spite of the fact that there is every evidence that the tissue pictured in Fig. 3 was in the remaining breast. When I examined this patient a few days before the operation, she had accidentally felt a lump four days before. Her attention was called to it when she struck her breast. Palpation of both breasts showed no evidence of chronic cystic mastitis. The breasts were not shotty, nor lumpy. There was no other tumor in this right breast nor in the other breast. It belonged to the group of a definite single tumor in one breast. The tumor was spherical, the size of a silver dollar, in the middle zone of the upper hemisphere, extending a little below the nipple. It was freely movable and fluctuated. It was diagnosed a cyst. The woman was unmarried, aged fifty, and still

menstruating. If this patient were examined today and the breast transilluminated, we would have seen no shadow and we could have made a pretty positive diagnosis of a benign tumor, because no tumor of that size, if solid, would transilluminate clear, and no cyst containing blood or thick, grumous material, would transilluminate clear. When I explored the tumor I exposed a typical blue-domed cyst beneath the subcutaneous fat. When opened it contained slightly cloudy fluid; the wall was smooth and thin. In excising it, the breast looked normal. We could not recognize, with the naked eye, what the microscope showed in Fig. 3. The



FIG. 11.—See text page 248. Case VI. Pathol. No. 43014. Photograph of gross section of breast tumor clinically malignant. Operation complete for cancer. Note the thin-walled cyst to the left and the thick-walled to the right. For sections see Figs. 12 and 13.



breast was largely fibrous and fatty. There was a second blue-domed cyst no larger than the end of the finger. In cutting out some of the breast tissue containing the two cysts, we exposed no dilated ducts as we cut through the breast tissue beneath the nipple, nor could we express from the normal ducts any material. On the gross



FIG. 12.—Case VI. Pathol. No. 43014. Low-power photomicrograph of thin-walled cyst shown in Fig. 11. Diagnosed (Bloodgood) benign.

pathology alone, nothing more was done, although the woman was fifty and unmarried. The microscopic study revealed that the cyst had no epithelial lining, but in the zone of breast there was evidence of fully developed chronic cystic mastitis in which these large, solid duct adenomas shown in Fig. 3 predominated.

This section has also been shown to a number of pathologists. In recent years the number who agree to its benignancy is increasing, but there is still a large minority who would advise at least the removal of the breast from such a frozen section.



FIG. 13.—Case VI. Pathol. No. 43014. Low-power photomicrograph of thick-walled cyst shown in Fig. 11. Diagnosed (Bloodgood) benign. (Thirty-eight pathologists diagnosed it malignant, thirteen benign.) See text page 248.

In 1921, when I studied 210 cases of single and multiple blue-domed cysts, there were, in less than 10 per cent. of the cases, microscopic pictures similar to that shown in Fig. 3.\*

Among these 210 cases of blue-domed cysts, only in a very few was the

\* Pathol. No. 26650, illustrated in the *Archives of Surgery* on page 502, Fig. 59.

complete operation performed because of frozen sections made at the time of the operation. When the breast was completely removed on exploring the blue-domed cyst, it was because the operator was of the opinion that the removal of the breast protected this patient from cancer. Statistical studies show that chronic cystic mastitis is practically always a bilateral condition, although the clinical evidence at the time of the first examination showed that it was present in one breast only. To be logical, therefore, one should remove both breasts. Or, again, the operator removed the breast to save the patient from a second operation for a new cyst. I have followed more than one hundred patients from whom we have removed a blue-domed cyst from one breast. None have developed cancer. It is now more than thirty years since the first case was observed. Less than 10 per cent. have had second operations because of the appearance of a new blue-domed cyst, but in the majority of cases the new cyst has appeared in the breast not previously involved. So that removal of the breast when one explores a blue-domed cyst is not logical—one should remove both breasts. The conclusions I made in the *Archives of Surgery* for November, 1921, on 210 cases is true today, nine years later, during which period we have had an almost equal number of new cases; and, in addition, when the blue-domed cyst is clinically a multiple tumor, we rarely operate at all or we explore one tumor to make the diagnosis positive. In recent articles since 1921 I have given further evidence to justify non-interference when there are multiple tumors of the cystic type in one or both breasts, that there is no indication to remove the breast when one finds at exploration one or more blue-domed cysts. But it is a good plan to make frozen sections of the wall so as to become familiar with the varying microscopic pictures. One, however, runs a greater risk, if frozen sections are made of the wall of a blue-domed cyst, of finding pictures which will influence one to be suspicious of cancer and lead one to the radical operation for cancer.

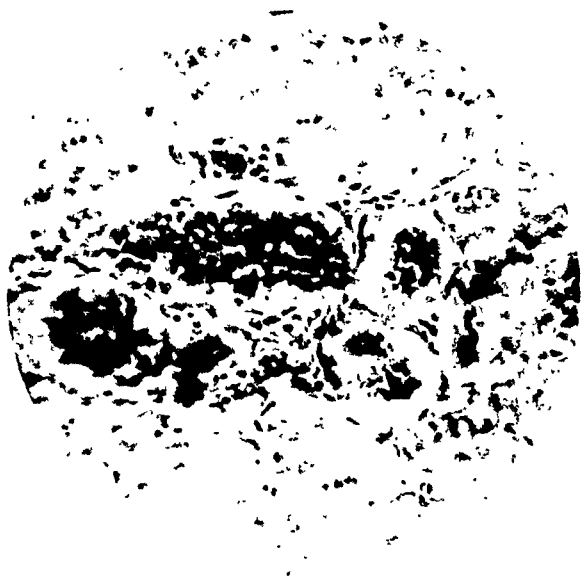


FIG. 14.—Case VII. Pathol. No. 25517. See text page 248. High-power of thick-walled cyst, similar to that shown in Figs. 11 and 13. Excised from breast seven years ago. No recurrence since. Pathologists differ as to malignancy.

*Cancer and Chronic Cystic Mastitis.*—In 1906\* I made a report on the type of chronic cystic mastitis which was even then known in the literature as Schimmelbusch's or Reclus' disease. These two authorities had published before 1900. None of us had many cases. As far as I can make out, Velpeau and Billroth, Paget and Warren, and other pathologists of the period before 1890 had either not seen, or had overlooked this type of chronic cystic mastitis in which the single or multiple larger blue-domed cysts are rarely present.

\* *Surgery, Gynecology and Obstetrics*, vol. iii, page 721, December, 1906.

These three contributions represented the beginning of intensive microscopic studies of lesions of the breast, because the modern surgery of the breast began in 1890.

There is ample evidence to prove that the conclusions of Schimmelbusch and Reclus that this diffuse, non-encapsulated, cystic adenoma or papillary cystadenoma of the breast was pre-cancerous, or associated with cancer in 50 per cent. of the cases, was due to the fact that it was difficult to differentiate in these early years between certain types of carcinoma and chronic cystic mastitis. It was repeating Velpeau's experience, who found that the young and not as yet experienced pathologists were making a microscopic diagnosis of cancer in lesions which he knew, from his vast clinical experience, were not cancer. I made the same mistake in 1906. Every case reported there either as malignant or suspicious of cancer proved, on further study, not to be cancer. The first case of Schimmelbusch's disease observed in Johns Hopkins Hospital was operated on by Halsted for cancer in 1892, clearly described in the gross and microscopic picture by Welch, but the glands were not involved and the patient is living today, thirty-eight years after operation. I described this lesion clinically and the gross and microscopic appearance in 1899. The case was identical with that described by Welch seven years before. I removed the breast, because everywhere I found these minute cysts filled with fluid or granular material, dilated ducts filled with pastille material. In spite of the conservative operation, the patient lived ten years and during this time had disappearing tumors in the remaining breast, and slight discharge from the nipple, but refused to return for operation.

In 1901 Doctor Finney removed the left breast with a typical example of diffuse Schimmelbusch's or Reclus' disease. The painting of the specimen by Horn\* is the best illustration in the literature up to date. An area in this breast was at first diagnosed adenocarcinoma and was used as an argument in favor of a close relationship between this variety of chronic cystic mastitis and cancer in my paper in 1906. But this patient lived nineteen years without recurrence. One other case, reported at that time, diagnosed cancer, in which the breast was first removed followed by the complete operation for cancer after the microscopic study, lived seventeen years.

Our studies of chronic cystic mastitis and its possible relation to cancer have continued since the publication in the *Archives of Surgery* in 1921, and at the present time confirm the statements made there. Doctors Copeland and Geschickter, in the Surgical Pathological Laboratory, with the aid of the Garvan Chemical Foundation, and the Bloodgood Research Fund, are making a restudy of the entire breast material, and up to the present have found no evidence to retract any statement previously made in the literature by me since 1921. There is no doubt that, microscopically, various stages of chronic cystic mastitis, encapsulated and non-encapsulated cystic adenoma, old fibroadenoma, rapidly growing intracanalicular myxoma, all forms of tubercular and pyogenic mastitis, and changes in the breast after recent injury, must be

\* *Archives of Surgery*, *loc. cit.*, page 468, Fig. 23.

looked upon as border-line breast lesions, because many well-trained pathologists, when confronted with the microscopic picture either in frozen sections in the operating room, or later in permanent sections, are inclined to the diagnosis of malignancy and advise at least the removal of the breast. In 1915 I submitted a large number of such cases to pathologists in a number of cities, and in not a single instance was there a uniform diagnosis, and on the whole, the majority favored the conclusion that the breast lesion was microscopically cancer or suspicious of cancer and advised the removal of the breast, or the complete operation for cancer. All these patients on whom the pathologists disagreed in 1915, fifteen years ago, are either living today with no evidence of cancer, or have died in the interval of other causes without evidence of cancer.

Fortunately the delay in finishing this paper allows me to review briefly the recent pathological gathering in the Surgical Pathological Laboratory of the Johns Hopkins Hospital.

During two days of morning and afternoon sessions, over fifty surgical pathologists interested in frozen sections in the operating room reviewed sections of eleven breast lesions. In our opinion ten were benign and one was malignant. However, on every case, except a distinctly benign adenoma of the breast, there was disagreement. When we compare the results in 1930 with those in 1915, we can make this statement: In 1915 the majority diagnosed malignant; in 1913 the majority diagnosed benign.

*Illustrative Cases.*—CASE I.—Pathol. No. 228. (Fig. 1.) Wall of a chronic lactation mastitis abscess diagnosed at Johns Hopkins in 1894 carcinoma. At the pathological conference in 1915, the majority favored carcinoma. In 1930 the minority favored carcinoma. Living today, no recurrence.

CASE II.—Pathol. No. 1734. (Fig. 2.) Diagnosis at Johns Hopkins in 1897, adenocarcinoma. First removal of non-encapsulated area of cystic adenoma. Permanent sections diagnosed adenocarcinoma. Complete operation—no metastasis to glands. Patient lived free from recurrence fifteen years. Majority diagnosis in 1915, malignant; in 1930, benign.

CASE III.—Pathol. No. 26650. (Fig. 3.) (See page 237.) This section is from the wall of a blue-domed cyst which I removed in 1920, ten years ago. This section was found later in the laboratory and was diagnosed benign. Remember only the cyst and a zone of breast were excised. At the present date (1930) the patient is well and both breasts are normal. In these ten years this section has been shown to many pathologists. The majority diagnosed it malignant.

It was not submitted to the group in 1930 as we did not have enough tissue to make fifty sections.

Those interested in border-line tumors are referred to my article in the *Archives of Surgery* for 1921 which contains a number of microscopic illustrations, the majority of which have been diagnosed malignant by a varying per cent. of pathologists. But in the ten years since that article was written none of these patients have exhibited any signs of cancer, whether the operation was excision of the tumor, or the breast, or the complete operation for cancer.

*Illustrative Cases Studied by Fifty or More Pathologists at the Meeting in the Surgical Pathological Laboratory in June, 1930.*—CASE IV.—Pathol. No. 42770. (Figs.

4, 5 and 6.) The actual sections were examined at the same time by the visiting pathologists in June, 1930. Twenty-two voted benign, twenty-five malignant. This patient was operated upon by my colleague, Dr. Thomas S. Cullen, at the Church Home and Infirmary Hospital. The adult patient had a single tumor, clinically benign. When explored, it was a non-encapsulated area in the breast containing solid areas and of a gross appearance not suggesting scirrhus carcinoma. As the frozen section was interpreted differently by Doctor Cullen and his associates, the tumor only was removed and the sections referred to me that day. The area shown in Fig. 4 is the type of solid adenoma or papillary cystadenoma, non-malignant. The majority of the tumor had this picture. In another area cysts predominated. Fig. 5 is a low-power and Fig. 6 a high-power photomicrograph of solid areas which in my opinion should be interpreted as malignant. All of the workers in the Surgical Pathological Laboratory agreed with this. Doctor Cullen performed the complete operation for cancer. Careful examination of the glands in the axilla showed no metastasis. Some of the pathologists made these statements: The tumor is benign, remove the tumor only. The nomenclature of the benign tumors varied—duct adenoma, benign cystadenoma; benign cyst adenoma with chronic mastitis. The majority of those who diagnosed the lesion benign advised the removal of the tumor only; two, the removal of the breast. Among those who diagnosed malignancy, all who advised operation advised the complete operation. One diagnosis was suspicious of malignancy, and the advice was to remove the tumor and carefully watch the patient.

In the discussion, I am convinced, everyone looked upon this case as very difficult to diagnose. I was surprised that so many—twenty-two out of twenty-five—concluded that the tumor was benign and suggested that the tumor only be removed.

CASE V.—Pathol. No. 42546. (Figs. 7, 8, 9 and 10.) In this case my associate, Dr. L. Clarence Cohn, explored the tumor because it was clinically distinctly benign. When he removed it (Fig. 7) there was a small blue-domed cyst surrounded by a few other minute cysts. A short distance from the larger cyst there was a zone of breast that impressed him as suspicious of malignancy. Fig. 8 is a frozen section from the cystic area and shows no evidence of malignancy. Fig. 9 is a low-power, and Fig. 10 a high-power photomicrograph of the solid area of breast tissue which Doctor Cohn, and the surgical pathologist at St. Agnes Hospital, interpreted as malignant and performed at once the complete operation for cancer.

These sections should be compared with Figs. 5 and 6.

The vote on this case of Doctor Cohn's was twenty-two benign and twenty-five malignant.

It is my opinion that in Doctor Cullen's and Doctor Cohn's cases it was safer to do the complete operation for cancer, but the chances are that these patients will live, and we will never know whether the lesion was benign or malignant. But as yet, until we get a differential stain, it is safer for the patient, when in doubt, to perform the complete operation for cancer.

CASE VI.—Pathol. No. 43014. (Figs. 11, 12, 13 and 14.) This case is of great interest. The tumor palpated like two or more nodules of different sizes, each feeling like a cyst, and the breast tissue around these nodules suggested malignancy. The entire mass was freely movable in the middle zone of the breast, and when moved in certain directions, the skin over it dimpled. There was, however, no change in the nipple. On transillumination there was a dark area distinctly smaller than the palpable mass. The dark area excluded the conclusion of multiple blue-domed cysts with thin walls. As the patient was past fifty and of a very nervous disposition, I decided to do the complete operation without exploration. Doctors Stewart and Cohn, at the examination in the office, and the internes at St. Agnes Hospital agreed with me that we should class this nodule as clinically malignant. Fig. 11 is a photograph of what we found when we bisected the breast in the region of the nodule. The mass to the left is a typical, smooth,

## BORDER-LINE BREAST TUMORS

thin-walled, blue-domed cyst surrounded by breast tissue similar to that pictured in the middle photograph. This breast tissue had no evidence of malignancy. The second, smaller tumor was a thick-walled cyst, with clear contents, smooth lining which undoubtedly produced the dark area on transillumination. There is nothing in the wall of either cyst or the breast tissue to suggest malignancy. Fig. 12 is a section from the thin-walled cyst, and Fig. 13 from the thick-walled cyst. Fig. 14 is the high-power taken from the wall of another thick-walled cyst, and presents an accurate picture of the histology in the thick-walled cyst, Fig. 13. All of us in the Surgical Pathological Laboratory looked upon this cyst, even the thick-walled one, as benign. The cyst shown in Fig. 14 was a thick-walled cyst removed seven years ago, and the breast saved. There has been no trouble since. In spite of this, thirty-eight of the pathological group voted it malignant, and thirteen benign. That is, more voted for malignancy than in Case V.

### CONCLUSIONS

There is no question that the number of border-line breast lesions is on the increase, and that the most expert pathologists today disagree when sections are submitted to them and all have equal opportunities to make the diagnosis. There may be an improvement in 1930 over 1915 but it is not sufficient to solve the problem. The surgical pathological laboratories connected with standard hospitals should be given more financial support, so they may be able to join in the search for a differential stain and give more time to meeting their colleagues in the group study of border-line lesions.

I hope shortly to publish, with full illustrations, the border-line tumors of the breast which we have collected now in the past forty years.

# GIANT INTRACANALICULAR MYXOMA OF THE BREAST

THE SO-CALLED CYSTOSARCOMA PHYLLODES MAMMÆ OF JOHANNES MÜLLER

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IN 1838 Johannes Müller collected several specimens of an unusual mammary tumor characterized chiefly by its large bulk, rapid growth following years of dormant quiescence, benign nature and peculiar gross and microscopic features. He considered this tumor as a neoplastic entity, and gave it the name cystosarcoma phyllodes.

Cystosarcoma phyllodes mammæ was an uncommon tumor even one hundred years ago. It is much less frequent now because the precursory fibroadenomas of the breast are recognized and removed and therefore the physician today does not see so many neglected advanced cases of mammary tumor. During the last twelve years at the Memorial Hospital the Breast Department has had the opportunity of studying four of these unusual tumors. A thorough perusal of medical literature covering the last century has furnished us with a total of 105 additional case reports; the present study, therefore, is based on an analysis of over 100 of these uncommon tumors.

This tumor is not peculiar to the human species as Bertolet reported the occurrence of a large tumor of one year's duration which was situated in the lower left iliac mammary gland of a nulliparous greyhound with cystic degeneration of the ovaries. In this instance the tumor was composed of multiple cysts which were almost completely filled by firm, fleshlike proliferations projecting from the cyst walls and which resembled sarcoma in its histological structure.

The tumor which Johannes Müller termed "cystosarcoma phyllodes" has been designated by at least twenty-five synonyms. It has been known also as "cystosarcoma papillare," "cystosarcoma arborescens," and "cystosarcoma polyposum intracanalicular." Sir Astley Cooper in 1829 included these neoplasms in his group of mammary tumors classified as "cellular hydatids." Sir James Paget called them "glandular proliferous cysts," and Thomas Hodgkin spoke of them as "composite cystoids." Cæsar Hawkins labeled them "tuberous cystic tumors of the breast." Schuh, in 1860, included them as a variety of "gelatinous cystosarcoma." Sir Benjamin Brodie in 1846 gave them the appellation of "sero-cystic sarcoma." Virchow in 1863 used the designation "intracanalicular myxoma"; Dietrich—"fibroadenoma intracanalicular fibromatosum"; Leser in 1888, and Noetzel in 1893—"fibrocystadenoma intracanalicular." Ziegler in 1889 used three different terms, namely, "cystofibroma papillare," "sarcome rameux" and "intracanalicular myxoma." Haeckel in 1894 diagnosed such a tumor as "cystoma papilliferum

mammæ." Beneke considered this tumor as an "adenoma pseudosarcomatodes"; Kreibitz likewise stressed the point that these cystosarcomas are really "pseudosarcomas." De Quervain in 1908 and Theile in 1909 called the benign tumor of this variety "fibroadenoma phyllodes" and changed the name to "fibrosarcoma phyllodes" in those instances where in the connective tissue stroma proved to be malignant. Frangenheim in 1930 also designated this tumor as "fibrosarcoma phyllodes." Wohlsecker diagnosed such a tumor as "fibromyxoma intracanalicular obliterans" because of the tendency of the connective tissue to obliterate the cysts or ducts. Bunkert used the descriptive term "fibroadenoma intracanalicular sarcomatodes xanthomatodes." Wilms adjudged this tumor to be a congenital variety of "adenomyxoma" whereas Coenen considered it as one of the "mutation" tumors. Ewing explained the etymology of the term "cystosarcoma phyllodes" as applied to tumors showing a branching system of more or less parallel cysts recalling the veins of a leaf.

Inasmuch as the neoplasm is usually not malignant the word "sarcoma" cannot be justifiably employed. We have retained the name "cystosarcoma phyllodes" because its usage for a hundred years has inseparably associated it with this tumor. In modern terminology a suitable descriptive term would be "giant intracanalicular myxoma of the breast."

*Gross Pathologic Anatomy.*—Sir Astley Cooper reported several cases of hydatid disease of the breast but all were not cystosarcoma phyllodes. His original description of hydatid disease (second type) corresponds to cystosarcoma phyllodes:

"The breast was enlarged and in the greater part hardened by the effusion of fibrine (coagulable lymph) in lobes into the cellular tissue; but in several parts it contained bags of serum and formed fluctuating cysts of various sizes. In each of these cells there hung a cluster of swellings like polypi, supported by a small stalk; and the little pendulous projections appeared to float in the fluid which had been produced around them in the different cysts.

"If one opens the clefts one finds communicating cysts, from which one can lift out large or conical and smooth or anastomosing and warty or villous excrescences, which somewhere adhere with a narrow or broad pedicle to the wall and continuously emerge with the connective tissue. (Virchow.)

"The dendritic intrusions into the cyst may occur at one point only, at several points, or, lastly, at all points simultaneously. In the last case, they converge, coalesce and eventually fill the entire cyst determining thus its aggregate structure. (Müller.)"

It is evident that Müller and Virchow as well as other early writers encountered much later stages of these neoplasms than are now commonly seen. Grossly the tumor tends to fall apart because of the enormous clefts and polypoid masses. On hemisection of such a tumor the intracystic contents are frequently packed so tightly that when the polyps are lifted out of the cyst they cannot be replaced. These polypoid projections may be described as cone-shaped, nodular, sessile, papillary, cauliflower, warty, arborescent, lamellar, teat-like, fingerlike or mushroom. These intracystic polypoid masses have been referred to as "papillary elephantiasis." Virchow. Orth



and Ribbert compared this tumor to a cabbage because of its frequent laminations; on section, layer after layer of flattened lamellæ can be removed. The polyps are visible to the naked eye, sometimes projecting from broad pedicles into the cysts with dendritic fimbriated extremities resembling a cock's comb. On pressure the polyps mutually flatten each other, which so distorts them that they become tortuous. Some of the polypi are flat and arranged like the leaves of a book. The polypi may become adherent to the opposite wall.

The masses may fill the clefts so well as to simulate a solid tumor. On cut section some areas appear solid like sarcoma and microscopically may be pseudosarcomatous. The anastomotic clefts appear as sinuositities; these clefts are the old dislocated cavities of the ducts. Such lacunar slits in the tumor substance are supposed to be diagnostic of a benign neoplasm. The cystosarcoma phyllodes may be multilocular; the cysts are often confluent due to rupture of intervening septa.

Only a thin layer of straw-colored fluid may exist between the vegetations and the cyst wall. In other instances the secretion is mucous, gelatinous, oily or resembles old extravasated blood; at times the fluid is granular due to its content of keratinized flakes. The liquid is a secretion of the epithelium of the cysts, modified by long residence in the cysts; leucocytes are frequently present.

The stroma is commonly myxomatous, and seems loose and gelatinous. It may be smooth, striated, glistening, yellowish-white, gray or reddish-gray and telangiectatic. Occasionally hæmorrhages occur from the delicate blood-vessels in the tissue stroma. The capsule of the tumor may be highly vascular, thin and transparent. The tumor does not invade the adjacent breast tissue and thereby lacks the destructive ability of malignant neoplasms. The neighboring breast tissue frequently contains enlarged, dilated ducts, presumably caused by pressure. In the same or opposite breast other fibroadenomas may be seen in various transitional stages of gelatinous metamorphosis.

*Pathologic Histology.*—The giant intracanalicular myxoma, in common with the intracanalicular fibroadenoma, derives its stroma from the subepithelial connective tissue (mantle tissue) that exists between the epithelial cells and the elastica. When such tumors are studied it is realized that the bulky stroma is not simply an increase of connective tissue but has characteristic qualitative changes as well. It is a heteroplastic type of interstitial connective tissue proliferation. The myxomatous character of the stroma is the most constant feature in cystosarcoma phyllodes. When the metamorphosis occurs with replacement of the connective tissue by myxomatous tissue, then the tumor increases rapidly in size. This is an expansive rather than an infiltrative growth. Only certain lobules of the tumor become myxomatous. These myxomatous changes are more pronounced within the polyps than in other interstitial tissues of the tumor. Under the microscope

these regions have the appearance of an interlacing meshwork of star-shaped cells and fibres.

The tumor cells are often radially arranged around the blood-vessels. This perivascular distribution is also seen in sarcoma. The spindle cells of the stroma tend to run parallel to the elongated clefts. The firm portions of the stroma are composed of fusiform cells with bizarre nuclei, which are narrow and rod-like, resembling smooth muscle nuclei. The variability of the size of the stroma cells and nuclei resembles sarcomatous tissue. However, mitoses are rare in cystosarcoma and true atypical cells are lacking. Jungst asserted that this periglandular metaplastic tissue was degenerative because he found the nuclei of the cells to be bare.

Bulky necrosis is never common, as occurs in true sarcoma. The blood-vessels of the stroma are delicate and embryonal; perivascular infiltration of lymphocytes and plasma-cells may be seen; many of the blood-vessels are thrombosed. Cholesterin crystals are sometimes seen between the tumor cells. Giant foreign body cells with multipolar kinesis engulf these cholesterol crystals. Some of the giant cells contain intracellular, doubly refractive fat which has been attributed to abnormal metabolism. Just as xanthomatous changes are frequent in degenerating breasts, so they are often seen accompanying inflammatory changes in these tumors. Hyalin changes occur diffusely, thereby decreasing the vascularity of the tumor. Hyalin metamorphosis affects particularly the polypoid tissue and the individual polypi decrease in size in this hyalin degeneration because of lessened œdema. The hyalin may become delimited in the centre of the polyps to form definite hyalin beads. Russell bodies are products of hyalin degeneration and are occasionally seen in these tumor cells. Calcareous deposits and pigment accumulation may occur in the stroma of the tumor.

The ducts of the tumor are so dilated and tortuous that no one microscopical section can ever show the entire course of one duct. The ducts become tortuous because of the connective-tissue invaginations. The ducts are the dividing tracts of the connective tissue. These very narrow ducts may grow into pseudosarcomatous structure; however, they do not form true acini. In no place is there ever any independence of the stroma proliferation from the ducts.

Not all of the polypi are covered with epithelium as some have become denuded by pressure or irritation. The majority of these giant intracanalicular myxomas have clefts lined by cylindrical or cuboidal epithelium. This cuboidal or columnar epithelium of the clefts may undergo metaplasia to form pavement epithelium, even true epithelial pearls, indicating a functional stability.

*Genesis.*—Mention should be made of the close relationship existing between terminal ducts, alveoli and their enveloping stroma. For instance, the stroma surrounding the terminal ducts and alveoli in the normal breast is relatively cellular and nonfibrous, whereas around the larger excretory

ducts the stroma is dense and fibrous.. It seems, therefore, that the connective tissue shares in the functional activity of the terminal ducts and alveoli. In the development of intracanalicular fibroadenoma and in giant intracanalicular myxoma, a controversy arose concerning which tissue was primarily at fault, the epithelium or the connective-tissue stroma.

Kurn, Leser, Von Saar, Schimmelbusch and Beneke believed that these tumors have their primary anlagen from the epithelium of the glands and that the changes in the connective tissue are secondary. On the contrary, Langhans, Klotz, Berka, Sasse and Virchow considered the important factors in the histology to be marked proliferation of the pericanalicular connective tissue, with secondary passive increase of epithelium. Haeckel maintains that the ducts dilate first with a consequent invagination by connective tissue. Harpeck ascribes the formation of these intracanalicular tumors to an enlargement of the excretory and milk ducts along their longitudinal ridges. Ziegler considers the cystic formation as merely the product of the connective tissue proliferation, whereas Mornard and Masson mention the possibility of origin in galactoceles. Beneke claims that this tumor owes its development to a blastomatosis of epithelium which may occur at any time in life, and the type or degree of stimulation which this epithelium is supposed to communicate to the connective tissue is unknown, but it seems to be delimited somewhat (although irregularly) to the stroma about the walls of the ducts.

In many lactating and resting breasts there is a metaplasia of the periductal and periacinar tissue into myxomatous tissue. When the duct dilates this myxomatous tissue presumably pushes the epithelium inward by an invagination and becomes papillary by budding. Later the cystic dilation may be so great as to surround almost the entire projection forming a cyst. (Jungst.)

*Age.*—The giant intracanalicular myxomas of the breast usually develop from preëxisting intracanalicular fibroadenomas. Intracanalicular fibroadenomas occur in the breasts of women who are generally older than those in whom occur the pubertal fibroadenomas which develop from the pericanalicular and periacinous connective tissue. The average age of the 109 patients with cystosarcoma phyllodes was 44.6 years; single women averaged 45.3 years of age. The average age of 151 patients at the Memorial Hospital with fibroadenomas of the breast was 35 years; single women were 12 years younger than the married women who had this particular tumor. The average known duration of cystosarcoma phyllodes in this series was 6.7 years; therefore, when this figure is subtracted from 44.6, the average age of the patients, we obtained 37.8 years, which is the estimated average age when the tumor first appeared. This age of onset is not significantly greater than the normal incidence for mammary fibroadenomas. Sometimes this tumor originates shortly after the onset of puberty. For comparison it is of interest to note that the average age of 2663 patients with glandular

carcinoma of the breast was 51 years and of eighteen patients with true sarcoma of the breast the average age was 47 years.

*Sex.*—Wülfung has maintained that no typical case of cystosarcoma phyllodes of the male breast has ever been reported, whereas Helmuth said that this tumor has occurred a few times in the male breast. Three of the 109 patients reported in this series were males, constituting an incidence of less than 3 per cent. of all cases.

*Trauma.*—The influence of trauma was mentioned in thirty-one case reports. Of these, eighteen patients stated that no trauma had been experienced, whereas thirteen other subjects gave definite histories of injury to the involved breast. These occurrences seemed authentic as the histories state that the tumors began to grow within certain definite periods after the dates of injury. However, there is no evidence to prove that a small precursory and undetected fibroadenoma did not exist prior to these traumas. In several instances the neoplasms appeared to exhibit an increased rate of growth, presumably due to stimulation by trauma.

*Etiological Influence of Lactation and Pregnancy.*—Finsterer concluded from his study of eighteen cases that cystosarcoma could be expected to develop in breasts which have reached the climax of physiologic function by repeated births and lactations. Helmuth, on the contrary, observed that they usually appear in the breasts of unmarried and childless women. It is our opinion that repeated births and lactations are the most frequent stimuli to the metamorphosis of fibroadenoma into cystosarcoma phyllodes. It is generally well known that the ordinary fibroadenoma participates in the hypertrophy which the breast undergoes during pregnancy and lactation. Moreover, the histories of these patients state definitely that the tumor acquired a marked growth impetus during pregnancy, lactation and menopause. Physiologists have long known that whenever there is functional proliferation of epithelium in the sexual cycle such as in the breast and uterus, there is a corresponding activity often expressed in mitosis in the stroma adjacent to the epithelium. In a similar manner the stroma of the intracanalicular fibroadenoma participates in the stimulation by pregnancy and lactation.

In ninety-one instances the marital state of patients in this series was given; fifteen only (16½ per cent.) were single. In thirty-eight reports the number of children was stated; nine had one child, eight had two, six had three, one had four, two had five, five had six, two had seven, two had eight, and three had ten children. On analysis we find that the average mother in this group had four children. Several of the cases illustrate the significance of these factors. One patient, a para two, and another, a para six, had never nursed. A third patient nursed her children from her normal breast but never from the breast in which the tumor developed because of deficient secretion. Another woman, a para six, nursed her children on the left breast only, the tumor developing later in the right breast. One

patient, a para six, observed that with each pregnancy the tumor would increase in size, but would remain quiescent during the non-pregnant intervals; she never nursed from the breast containing the tumor because of a retracted nipple, although this breast lactated at the completion of each pregnancy. In another instance the tumor became swollen with each menstrual period. Two patients volunteered the information that lactation stimulated the growth of the tumor. Another woman was pregnant at the time the tumor was extirpated. Still another had only one child, nursed this child and later served as a wet nurse for two other children. In a thirty-



FIG. 1.—Case report by von Graefe (1838). The patient was a Russian woman, thirty-nine years of age. She had nursed her five children without lactational difficulties. After her last childbirth, a small nodule the size of a filbert (fibro-adenoma?) was felt in the right breast. This nodule never increased in size. In 1836, a new tumor appeared in the left breast and grew slowly until 1838, when it exhibited an increased impetus of growth. It ruptured spontaneously and twelve hours later a large cauliflower vegetation prolapsed through the ruptured skin. This enormous tumor covered the entire chest, displaced the right breast and a local mastectomy was done without anæsthesia. While an assistant supported the breast, two surgeons with three knives amputated the breast by three slashes in less than thirty seconds. Immediate hæmostasis was obtained by compressing nine large severed vessels between the fingers. The breast and its content of tumor weighed twenty-two pounds and eight ounces. A cure was effected.



FIG. 2.—Case report by Helmuth (1871). The patient was a woman, aged sixty-eight years, who first observed a small tumor in her right breast twenty years previously. This tumor gradually increased in size until it extended from the clavicle to below the waist and from the sternum beyond the axilla to the scapular line. The integument over the tumor was tense and bluish; the tumor mass was nodular, circumscribed and fluctuant. Treatment consisted entirely of injection of carbolic acid. The patient died several months later.

year-old woman menstruation ceased spontaneously; whereupon an arrested inactive fibroadenoma grew with great rapidity. A thirty-nine-year-old woman, para five, noticed the appearance of a tumor immediately after her last childbirth, which was followed by a sudden and permanent amenorrhœa.

*Symptomatology.*—The three clinical features which distinguish this tumor from other mammary tumors are the presence of a precursory tumor, rapid growth and attainment of unusual size. In Finsterer's eighteen cases, pain occurred in six instances; it was never present in the early stages but appeared only when rapid growth occurred with pressure and tension on the overlying skin. In our collective series the initial evidence in sixty-seven

women was the discovery by the patient of a palpable lump in the breast. Two patients stated that the initial sign was a discharge from the nipple; this is quite infrequent and is not the usual accompaniment of cystosarcoma phyllodes. Only four patients stated that pain in the breast was the initial symptom, but nineteen complained of the presence of pain in later stages of the disease. Seven women complained chiefly of the great inconvenience caused by the weight of these heavy tumors. Only eight of the 109 patients had a constitutional impairment of health. The general health remains good in spite of the tumor. Cachexia, loss of weight and anæmia never occur unless ulceration, infection and hæmorrhage alter the local condition.

*Physical Signs.*—The usual giant intracanalicular myxoma of the breast is a bulky, freely movable, encapsulated, non-adherent tumor with bosselated nodulations, variable regions of fluctuations and resistance unaccompanied by retraction of the nipple or palpable axillary lymph-nodes. The lobulations and inequalities of the tumor are easily felt through the skin. The smallest tumors are smooth, even and regular in shape; occasionally they are disc-shaped. Fluctuation is frequently elicited in the superficial cysts. Unequal consistence of the tumor, some portions elastic and other parts firm and knobbed, is an important distinctive feature. A simple fibroadenoma may be found concomitantly in the opposite breast or in the same breast with the cystosarcoma phyllodes. (Birkett.) Semb reported an instance wherein multiple cystosarcomas developed about as many multiple fibroadenomas. The axillary lymph-nodes are not involved in the disease process, but they may become enlarged by inflammatory changes when ulceration and infection occur in the breast tumor.

*Size.*—In Finsterer's series of eighteen cases four of the tumors were as large as a man's head. In our collective series, eighteen of the tumors were said to be as large or larger than a human head. The actual weight of nineteen tumors was given, averaging 7.6 pounds each. These tumors are usually larger than a closed fist and they may weigh as much as 20 kilograms. (Ribbert.) When the tumor attains a great size, the major portion of the growth has taken place in one year.

*Location.*—Of fifty-nine tumors in which the location was mentioned thirty-eight were in the right and twenty-one were in the left breast. In twenty-six cases the location in the breast was mentioned; twelve were in the upper outer quadrant, four were in the lower outer quadrant, three in the lower inner quadrant, two in the upper inner quadrant and five occupied the central region of the breast.

*Changes in the Skin of the Breast.*—In Finsterer's eighteen patients the skin was adherent to four of the tumors and ulceration had occurred in three instances. In our collective series the status of the skin was mentioned in sixty-five case reports. Twenty-one had ulcerated lesions at the time of examination; four of these ulcerations were attributed to trauma. Five other tumors were adherent to the skin. In the remaining thirty-nine patients the skin was not ulcerated nor adherent to the tumor. In five patients rapid

fungation occurred once the skin had ruptured; in one instance an enormous cauliflower growth extruding within twelve hours' time. The capsule of the tumor and the superjacent skin may be ruptured by pressure necrosis induced by tension. The fungations which frequently result are not indicative of malignancy. The ulceration occurs at the lowest part of the tumor or at the point of greatest tension. Infection inevitably follows ulceration and at times gangrene ensues. Prior to rupture the skin is usually tense, smooth, shiny, dry, red, livid, cyanotic or violaceous. Enormous subcutaneous veins, often as thick as pencils, may radiate from the superficial vascular part of the tumor like a *caput medusæ*.

*Nipple*.—Retraction of the nipple is so very unusual that when it does occur the examiner suspects carcinoma rather than cystosarcoma. Poulsen emphatically declares that the nipple is never involved. In our collective series there is only one instance in which the nipple was retracted by the tumor; in another case the nipple was obliterated.

*Precursory Tumor*.—In fifty-seven of our collected case reports definite mention was made of a precursory tumor. Forty-seven of these patients gave a definite history of the presence of a precursory tumor in the breast. In ten instances a specific statement was made that no preëxisting tumor had been present according to the patient's knowledge.

*Duration*.—In Frangenheim's report the period of development averaged thirty-five to forty-eight months. In our collected series, there were seventy-five case reports in which this information was given. We found the average duration to be 6.7 years from the day of discovery to the date of examination. When these tumors exist for many years, they may remain inactive for a considerable portion of this time.

*Rate of Growth*.—Finsterer found cystosarcomas and true sarcomas to develop more slowly than carcinoma of the breast. The period between discovery and examination for these three tumors was given as follows: 25.5 months for cystosarcomas; 18.3 months for true sarcoma; 16.3 for carcinoma. True sarcoma of the breast was said to grow more rapidly than cystosarcoma. Helmuth in 1871 was the first to observe that cystosarcoma phyllodes grew with extreme rapidity with long intervals of arrested growth. The rate of growth was indicated in eighty-two of our collected case reports. In nine patients the tumor was of slow growth; on eight occasions the tumor grew at a moderate rate; in one instance the growth was slow with later a moderate increased rate; in twenty-six cases the tempo of growth was very rapid; in thirty-eight patients the tumors grew slowly or not at all for a long time and then exhibited sudden exacerbation of growth. In twenty-seven of these thirty-eight case reports wherein the actual time of the increased growth rate was mentioned, the average total duration of the tumor was 8.9 years, but the average time during which the tumor had shown the characteristic increased acceleration of growth was only 8 months.

*Cystosarcoma Phyllodes—a Benign Tumor*.—Cystosarcoma phyllodes is not a true sarcoma because it does not have a sarcomatous structure con-

sistently, it does not metastasize commonly to viscera and it seldom recurs locally. Wulff classifies this tumor as an entity somewhere between true sarcoma and simple fibroadenoma; he admits, however, that genuine and destructive sarcoma can develop in these tumors although it is commonly the sarcomatous type. Grohe made the statement that cystosarcoma phyllodes is as far removed from carcinoma as is condyloma of the penis. Schimmelbusch, Beneke and Haeckel emphasize the benign nature of cystosarcoma.

When the tumor perforates the skin it gives a false appearance of malignancy. The age of the patient, the rate of growth, the presence of pain and the occasional enlargement of the axillary lymph-nodes do not necessarily indicate a malignant neoplasm. Enlarged axillary lymph-nodes may be inflammatory.

It does seem, however, that sarcoma originates in cystosarcoma phyllodes more frequently than it does in the original fibroadenoma. Billroth reported two cystosarcomas which metastasized; however, there was insufficient microscopical description of these tumors to rule out genuine sarcomas. Theile's case report of cystosarcoma phyllodes mammae is unusual for although histologically verified sarcomatous metastases to bone occurred, sarcoma was not demonstrated in the primary breast tumor. Poulsen found that metastasis from true sarcoma of the breast occurred in 40 per cent. of patients, but observed recurrence or metastasis in only 25 per cent. of mammary cystosarcomas of all types. Prym removed a large breast tumor and after microscopical study in which no malignant areas were seen, diagnosed the tumor as cystosarcoma myxomatous phyllodes. Two peculiar areas were seen, one of cholesteatoma and another of peculiar fat lobules in the centre of the original tumor, said to have been composed of immature lipoblasts. The tumor recurred locally and then metastasized to the lungs. The pulmonary metastases contained no epithelial elements. Prym described the metastases as myxosarcomatous but in the accompanying microphotographs the appearance suggests liposarcoma as well as myxosarcoma.

Of ninety-one cases in our collected series in which the outcome was mentioned, there were but six recurrences; one patient died from pulmonary metastases after a simple mastectomy; in three patients simple mastectomies were followed by recurrences which were excised; in one patient a recurrence followed a radical mastectomy; and in another, a local excision of the tumor was followed by a recurrence which was removed by simple mastectomy.

*Differential Diagnosis.*—Hemisection of the surgical specimen in the operating room reveals a gross appearance which is absolutely diagnostic and cannot be confused with any other tumor of the breast. The intracystic polypoid lobulations with narrow, tortuous clefts are not simulated by any other tumor except the intracanalicular fibroadenoma.

The clinical differentiation from carcinoma is not difficult. No cancer could grow so large without involving the skin. The encapsulation of the tumor, the freedom of the nipple, the lack of fixation and other evidences of



infiltration are important diagnostic features. The mobility of the skin over the tumor, the absence of the orange-peel type of skin and of regional distant metastases, as well as the maintenance of good general health, are diagnostic points in which cystosarcoma phyllodes differs from cancer. The three varieties of breast cancer which bear a faint resemblance to this tumor are the diffuse ductal carcinoma, the bulky adenocarcinoma and the intracystic papillary carcinoma. In the first-mentioned carcinoma the breast is diffusely invaded, the tumor margins are not easily definable, the nipple is invariably retracted and the skin of the entire breast is thickened and œdematous. The bulky adenocarcinoma which occurs more often in elderly subjects metastasizes late and often invades and ulcerates the skin; it may closely resemble cystosarcoma phyllodes. The intracystic papillary carcinoma originating in cysts or dilated ducts is often preceded or accompanied by a sanguineous discharge from the nipple. It is occasionally multiple and once its capsule is ruptured has the ability to infiltrate.

The carcinosarcoma of the breast is sometimes referred to as adenosarcoma. Many of these tumors are enormous; they may weigh ten to twenty pounds. They often ulcerate through the skin and the epithelial elements may metastasize to the axillary lymph-nodes. The round-cell sarcoma of the breast, including the lymphosarcoma, is softer than cystosarcoma, grows with greater rapidity and is many times more radiosensitive when subjected to the therapeutic test of irradiation.

The mixed tumors of the breast, according to Wilms, are of teratoid origin, developing from embryonal ectoderm and mesenchyme which are included in the mammary gland. These tumors may contain epidermis, cartilage and other structures indicating their origin from multiple germinal layers. Others say the mixed tumor is a metaplastic derivative of a benign tumor; in this sense there may be a histogenetic relation to cystosarcoma. Clinically they cannot be distinguished from encapsulated benign tumors of the breast such as large fibroadenomas, adenomas and cystosarcoma phyllodes. They are usually well delimited, encapsulated tumors, which remain small for a long time, then grow with great rapidity. They cause atrophy of the mammary gland proper without invasion. They do not adhere to the deep tissues nor do they metastasize by lymphatic vessels. They elevate and render the skin tense but never directly infiltrate the skin. They occur at all ages from twenty to seventy years.

An analogy exists between fibroadenomas, cystosarcoma phyllodes and chronic cystic mastitis because they have the same histological elementary or primary changes. They are differentiated by delimitation (cystosarcoma and fibroadenoma), by proliferation of epithelial tissue (fibroadenoma) and of connective tissue (cystosarcoma phyllodes). Chronic cystic mastitis is a more diffuse process and has few of the clinical features of a giant intracanalicular myxoma such as the rate of growth and bulky size. Tuberculous mastitis and mammary actinomycosis may be ruled out by the clinical history,

## GIANT MYXOMA OF BREAST

by the physical findings upon examination and finally by an aspiration of the fluid content followed by microscopical diagnosis.

*Prognosis.*—The prognosis is usually good. It depends on: the type of cystosarcoma phyllodes, *i.e.*, whether cellular or myxomatous; the fixity of the tumor; the extent of the operation; the age and physical status of the patient; the presence of ulceration and infection; the duration and the size or local extent of the tumor.

*Treatment.*—The management par excellence is the prophylactic measure of removing all mammary fibroadenomas. If the tumors are small, local wide extirpation may be sufficient. If the tumor is incompletely removed it will recur. Billroth found that cystosarcoma phyllodes in young women

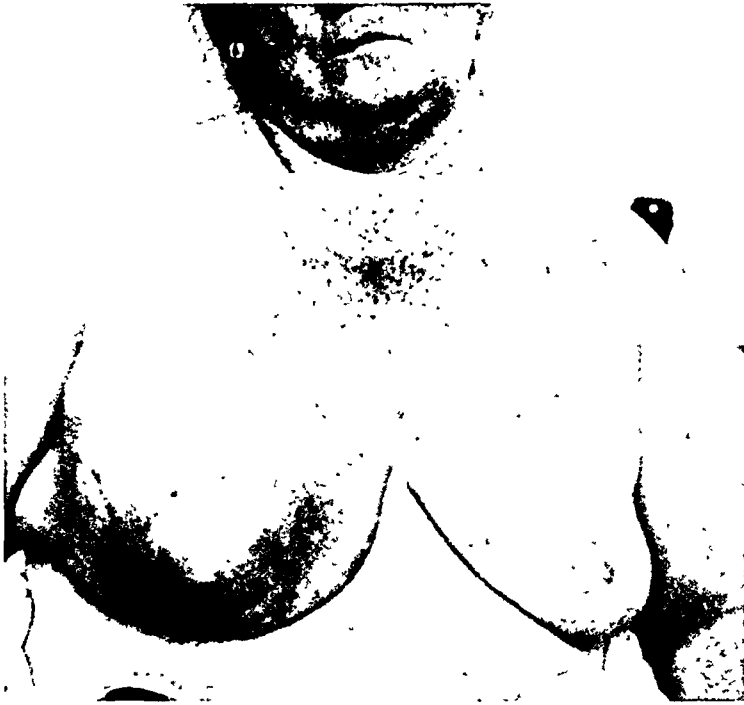


FIG. 3.—Case I. Clinical photograph. Note the bulk and delimitation of the tumor, the intact skin, the tortuous, dilated veins and the healthy appearance of the patient.

does not recur after removal but in older women (over thirty) he advises a more radical operation because of the danger of recurrence, or even transition to carcinoma. Such recurrences may be from residual portions of previous tumors or by the formation of new tumors. Hence it seems wiser in all cystosarcomas of considerable size to do a complete amputation of the breast, including the fascia over the pectoral muscles.

In ninety-one of our collected case reports the method of treatment is mentioned as follows: nine patients had radical mastectomies, forty-five had simple mastectomies, thirty-five had local excisions of the tumors, one had an intratumoral injection of phenol and another patient had a local mastectomy by the simple procedure of constricting the pendulous pedicled breast by a stout ligature.

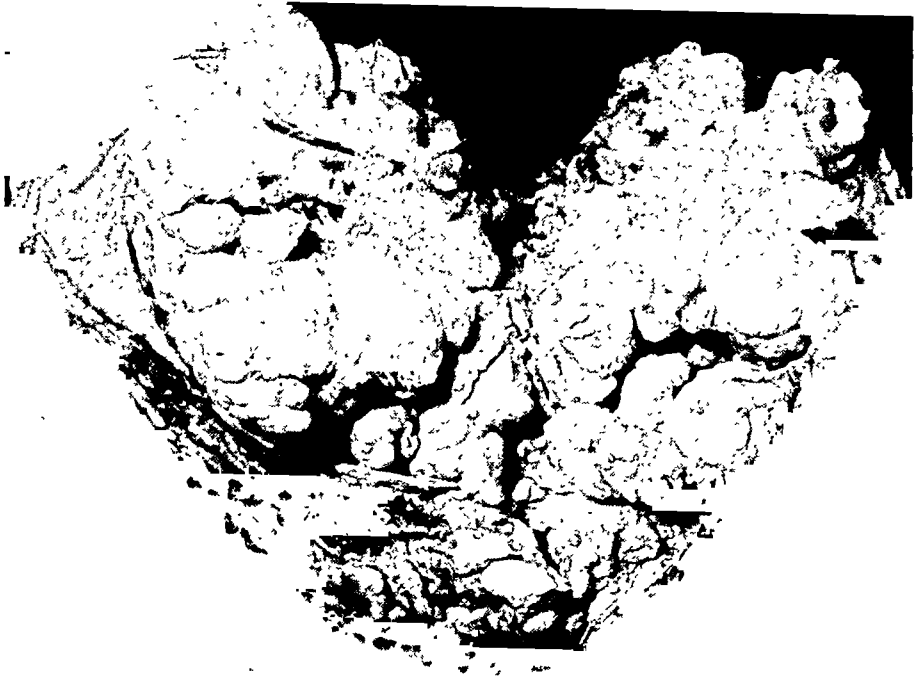


FIG. 4.—Case I. Gross specimen illustrating the large, intracystic myxomatous polyps separated by narrow, tortuous clefts.

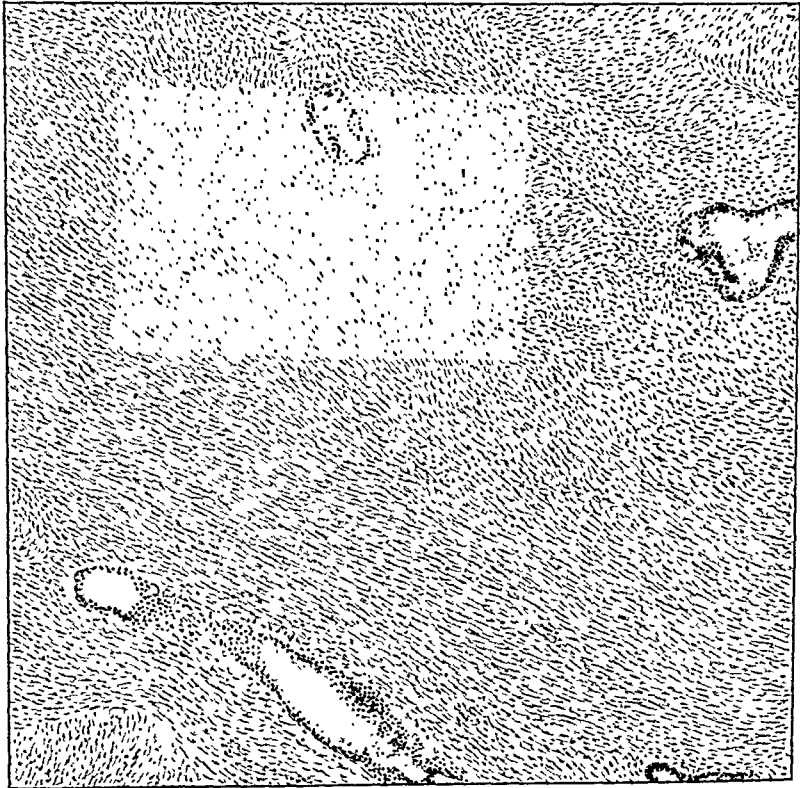


FIG. 5.—Case I. Densely cellular, pseudo-sarcomatous stroma surrounding glandular lacunae.

# GIANT MYXOMA OF BREAST

## REPORTS OF CASES OBSERVED AT THE MEMORIAL HOSPITAL

CASE I.—D. K., a white, married woman, aged fifty-six years, applied to the Memorial Hospital December 3, 1927, complaining of a bulky tumor occupying the entire right breast.

*Past History.*—The patient was a diabetic. She had seven children, each of whom was nursed for at least two years without any lactational difficulties.

*Present Illness.*—Thirty-seven years previously (1890), following her first child-birth, the patient noticed a small lump beneath the right nipple. This nodule remained inactive until one year ago when it grew rapidly to occupy the entire breast. One month prior to examination there was an intermittent discharge of blood from the nipple.

*Physical Examination.*—The entire right breast was the seat of a bulky, lobulated, cystic tumor mass. The nipple was flattened but not retracted. There was no skin adherence and the tumor was freely movable with the breast. A radiograph of the chest was normal; heart and lungs were normal. The blood sugar was 146 milligrams per 100 cubic centimetres of blood. There was persistent albuminuria. The clinical diagnosis was papillary cystadenocarcinoma of the breast.

*Treatment.*—The patient refused operation until May 11, 1928, when a local mastectomy was performed, using a transverse elliptical incision. At this time the skin had ulcerated and the tumor was fungating. Convalescence was uneventful. Two years later there was no evidence of recurrence.

*Gross Pathologic Anatomy.*—The entire breast was occupied by a tumor mass, measuring 15 by 11 by 10 centimetres in diameter. The nipple was normal but displaced. Two and one-half centimetres from the areolar margin was a large ulceration, excavated to a depth of one centimetre. The floor of the ulcer was formed by soft tumor nodules. The tumor was invested by a thick fibrous capsule, the inner coat of which was perforated in certain regions. The tumor was composed of firm pearly-gray, gelatinous, intracanalicular polyps, with foci of caseation and calcification. The clefts between the polyps were filled with a thick, greenish fluid.

*Pathologic Histology.*—The stroma was pseudosarcomatous due to its cellularity. There were many interlacing bundles of spindle and fusiform cells. In some regions, the glandular structures resembled the sweat glands of the breast. The epithelium lining the ducts was in several layers. There was an abundant perivascular lymphocytic infiltration. Other degenerative changes were observed in regions containing small hæmorrhages, hyaline metamorphoses and deposits of cholesterol crystals which were engulfed by syncytia of foreign-body giant cells.

CASE II.—B. S., a married Jewess, aged twenty-eight years, applied to the Memorial Hospital January 21, 1930, complaining of a rapidly growing lump in her right breast.

*Past History.*—Her father died with pneumonia at the age of seventy-nine years; her mother died of myocarditis at the age of sixty-four years. The patient had two children, aged four and two years. She nursed the first child thirteen months and the second child five months without any lactational difficulties.

*Present Illness.*—Three and one-half years previously (July, 1926), she felt a lump about 1 centimetre in diameter, medial to the right nipple. This lump remained inactive but persisted for three years until September, 1929, four months prior to admission, when the tumor began to grow with great rapidity and caused a peculiar dragging pain in the breast. She had not lost weight.

*Physical Examination.*—The patient was a well-developed, well-nourished white woman in good general condition. Her lungs were clear and resonant. Her heart was normal to physical examination. The liver was not palpable. The right breast was more prominent than the left and the central portion was occupied by a round tumor measuring 7 by 5 centimetres in diameter. The nipple was not retracted, the tumor was freely movable on the chest wall and the skin over it was not adherent. Its con-

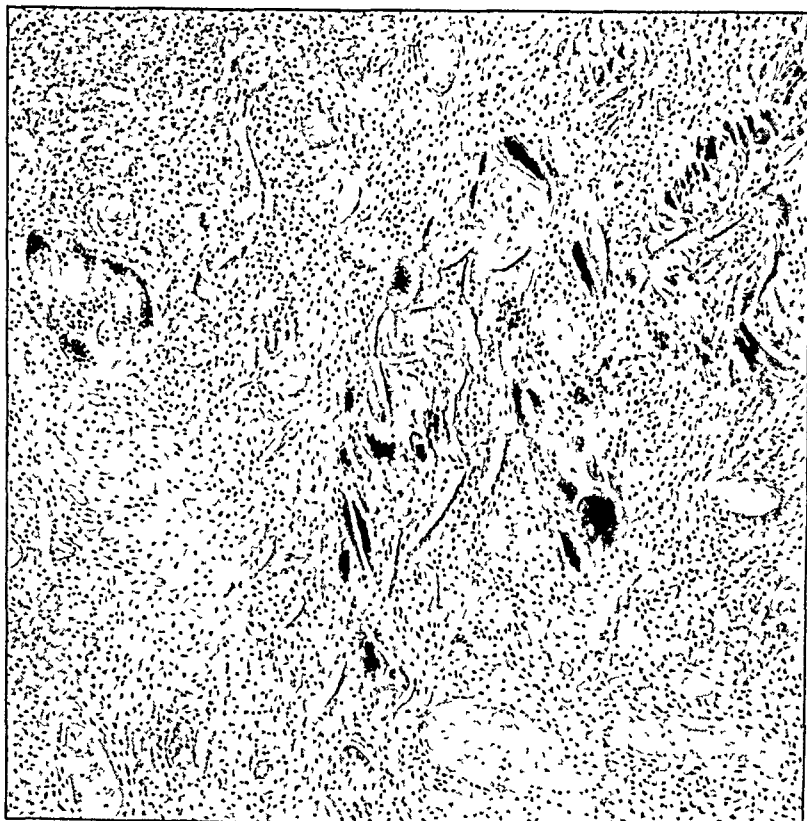


FIG. 6.—Case I. Xanthomatous region of tumor containing numerous crystals of cholesterol, engulfed by large, syncytial, foreign body giant cells.



FIG. 7.—Case II. In this gross specimen, the intracanalicular polyps are firm, gray and striated, containing discrete, small, interstitial hemorrhages.

## GIANT MYXOMA OF BREAST

sistence was firm and elastic. There were no palpable supraclavicular nor axillary lymph-nodes. The clinical diagnosis was fibroadenoma of the breast.

*Treatment.*—On January 31, 1930, a simple mastectomy was performed to include the pectoral fascia. Six months later there was no evidence of recurrence.

*Gross Pathological Anatomy.*—The tumor measured 9 by 7 by 5 centimetres in its diameter: Within its thick capsule were multiple-soft, white, gelatinous polypoid intracystic projections. The polyps were closely approximated. Some portions of the tumor were myxomatous, others fatty, and still others hæmorrhagic. The breast proper was not invaded.

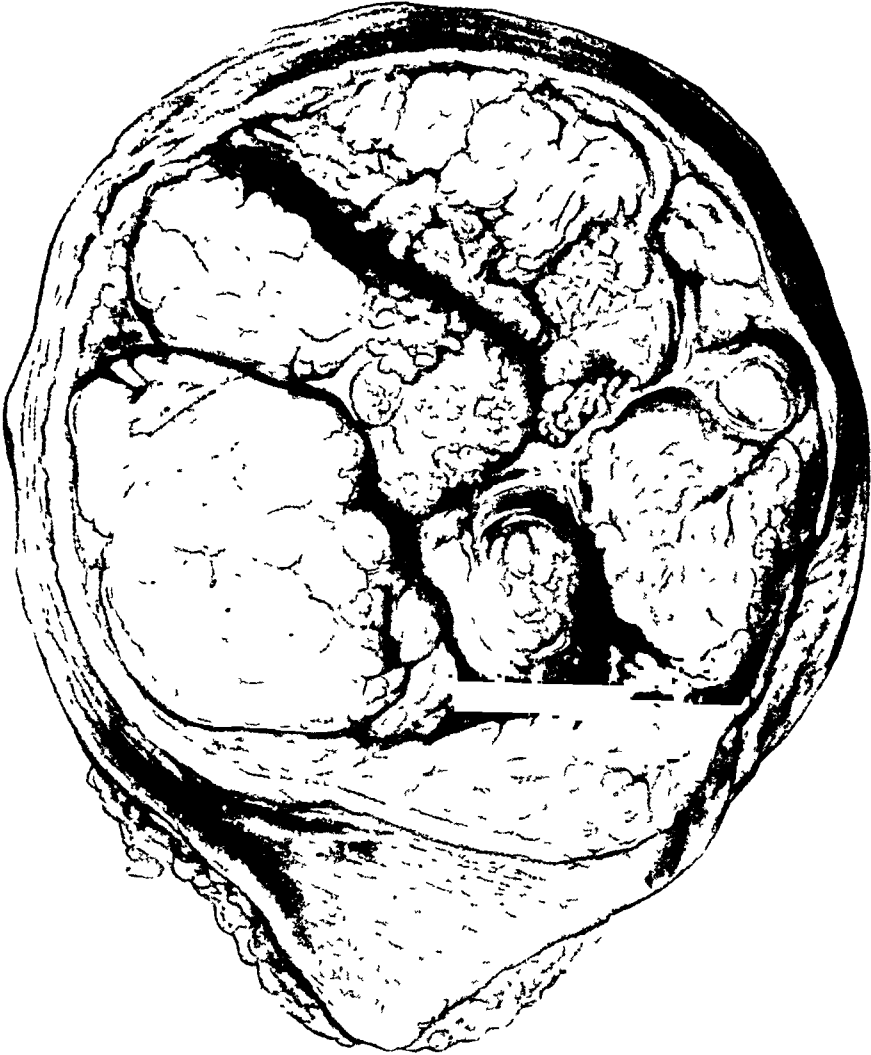


FIG. 8—Case III. The polypoid masses have the characteristic fimbriated, phylloidic or cock's comb appearance

*Pathologic Histology.*—The stroma throughout the tumor was diffusely myxomatous. There was some hyaline degeneration of the connective-tissue type, surrounding the enlarged veins. Small hæmorrhages in the stroma were in the process of organization. There was perivascular infiltration of large mononuclear leucocytes which contained an abundance of brownish-yellow pigment granules. The glandular elements were more common than in most cystosarcomas; the tumor could be properly called an intracanalicular myxadenoma. The tall columnar cells lining the ducts rested on a layer of flat basal cells. Many of the ducts were dilated and contained colostrum corpuscles. In some regions the ductal epithelium was of the sweat-gland type, with intraductular papillary tufts of large columnar cells with eosinophiles cytoplasm.

CASE III.—S. K., a married Jewess, aged thirty-four years, applied to the Memorial



FIG. 9.—Case III. Cross-section of a typical intracanalicular myxoma.



FIG. 10.—Case IV. This gross specimen exhibits the thin, delicate capsule, the multilocularity and the gelatinous character of the stroma of the cystosarcoma phyllodes.

## GIANT MYXOMA OF BREAST

Hospital April 21, 1930, complaining of a rapidly growing lump involving the entire right breast.

*Past History.*—Her father died of heart disease at the age of fifty-two years and her mother was living and well. There was no history of cancer nor of benign breast tumors in the family. The patient has always been obese; her weight was 180 pounds. She was under treatment for hypertension. She had one child, aged fifteen years; she nursed this child only one month because of an abscess in the right breast; this abscess was incised at the lower edge of the breast.

*Present Illness.*—Nine years previously (1921), she first felt a small lump in the upper central portion of the right breast. This mass remained about the size of a hen's egg for nine years without discernible enlargement. Three months prior to examination (January, 1930), the right breast was struck upon the corner of a table. Following this injury there was ecchymosis over the upper part of the breast and the preëxisting lump began to enlarge very rapidly. There was some initial transient pain. The patient did not lose any weight and remained in good general health.

*Physical Examination.*—The entire right breast was involved by a bulky, nodular, semi-fluctuant, well delimited, ovoid, freely movable tumor measuring 16 by 12 by 10 centimetres in diameter. The nipple was flattened but not retracted. The skin was slightly adherent at one point toward the medial edge of the breast. There were no palpable lymphadenopathies. The subcutaneous veins were quite prominent and distended over the inner segment of the breast. A radiograph of the lungs was negative for metastasis of carcinoma.

*Treatment.*—A cycle of four high voltage X-ray treatments was given over the right breast to include the axillary and supraclavicular spaces. There was only slight regression in the size of the tumor following these treatments. May 9, 1930, a right radical mastectomy was done using a transverse Stewart incision. The axilla was dissected completely and the pectoral muscles were removed with the breast. Three months later there was no evidence of recurrence.

*Gross Pathologic Anatomy.*—The tumor measured 16 by 10 by 9 centimetres in its diameters. Its capsule was distended and in contact with the skin of the breast. There was some spontaneous necrosis within the tumor, and the clefts contained a brownish fluid. The intracystic cauliflower projections showed regions of myxomatous, xanthomatous and fatty degeneration.

*Pathologic Histology.*—The histologic arrangement of the tumor was that of a typical intracanalicular myxoma. The myxomatous changes were limited to the periductal tissues. In some regions the stroma was densely cellular with fusiform cells of uniform type. There was also some calcareous degeneration and hyaline changes in the stroma.

CASE IV.—T. B., a single Italian woman aged forty years, had noticed a gradual progressive enlargement of both breasts during the last ten years. In the last few months the tumors in both breasts grew with great rapidity. She suffered an occasional dull pain in both breasts. Her menstrual history was normal; she had never been pregnant.

Her younger sister had a mammary tumor excised five years previously at another institution. This tumor was said to be a cystosarcoma phyllodes.

January 20, 1930, the tumors in both breasts were excised by Dr. M. Caturani, at the Parkway Hospital, New York. Convalescence was uneventful. There has been no recurrence. We are indebted to Doctor Caturani for permission to study this tumor.

*Gross Pathologic Anatomy.*—In the left breast the tumor measured 13 by 11 centimetres in diameters, and in the right breast the other tumor was the size of a small orange. Both tumors were encapsulated, lobulated, intracanalicular polypoid myxomas.

*Pathologic Histology.*—The gross architecture of the tumor resembled the well-known intracanalicular fibroadenoma. The myxomatous changes were not confined to the periductal tissue which forms the polypoid masses but also were found in the



deeper stroma. Many of the polyps had undergone hyaline metamorphosis, but retained their epithelial investments. Dilated, delicate, embryonal blood-vessels occupied the centre of these polyps, many of which were œdematous. The clefts were lined by two layers of epithelial cells, the flat basal-cell layer and a superficial epithelium as hyperplastic as to simulate intraductular carcinoma.

## SUMMARY

After a study of 109 cases of giant intracanalicular myxoma of the breast (cystosarcoma phyllodes), we may summarize the salient characteristics of this tumor as follows:

1. Great size, averaging 7.6 pounds.
2. Lobular shape, with variable regions of fluctuation and resistance.
3. Encapsulation.
4. Mobility and usual non-adherence to skin and fascia.
5. No retraction of nipple and no involvement of axillary lymph-nodes.
6. Possible occurrence in males (3 per cent.).
7. Development from preëxistent fibroadenomas, probably intracanalicular fibroadenomas.
8. Important rôle of lactation and nursing difficulties in this metamorphosis.
9. Long duration, averaging 6.7 years.
10. Long initial period of quiescence or slow growth, followed by sudden rapid acceleration.
11. Intracystic polypoid excrescences moulded by apposition with each other.
12. Narrow, sinuous, distorted clefts between the polyps.
13. Myxomatous stroma with cellular pseudosarcomatous regions.
14. Benignity; good prognosis with freedom from recurrence.
15. Successful treatment by wide local excision or simple mastectomy.

# THE RESULTS OF TREATMENT OF CANCER OF THE BREAST

BASED ON A STUDY OF 489 CASES—1914–1925

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FROM THE STATE INSTITUTE FOR THE STUDY OF MALIGNANT DISEASE

THERE is probably no other disease which the surgeon and radiologist are called upon to treat that is more discouraging, at times, than cancer of the breast. Professor Ewing<sup>1</sup> has summed up the difficulties in the treatment of this disease and I believe that a quotation of his statement is very timely: "From clinical and pathological studies I have drawn the impression that, in dealing with mammary cancer, surgery meets with more peculiar difficulties and uncertainties than with almost any other form of the disease. The anatomical types of the disease are so numerous, the variations in clinical course so wide, the paths of dissemination so free and diverse, the difficulties of determining the actual condition so complex, and the sacrifice of tissue so great, as to render impossible in a majority of cases a reasonably accurate adjustment of means to ends."

My experience leads me to agree with Doctor Ewing and I feel that those who have to deal with this group of cases must not be too optimistic, for pessimism is sure to follow when the vagaries and freakishness of the metastases manifest themselves. Every surgeon and radiologist has learned to regard cancer of the breast as being one of the most tricky and difficult diseases to prognosticate. Such eminent American authorities as Doctors Halsted,<sup>2</sup> Willy Meyer,<sup>3</sup> Greenough,<sup>4</sup> Bloodgood,<sup>5</sup> and Lee,<sup>6</sup> as well as such eminent foreign authorities as Mr. Handley,<sup>7</sup> Professor Wintz,<sup>8</sup> and Forsell and his associates at Radiumhemmet,<sup>9</sup> have at various times contributed greatly to the advancement of our knowledge of this disease. Handley's work on cancer of the breast, in which he so clearly demonstrates the channels of dissemination through the lymphatics, is a monumental contribution in the advancement of our knowledge. Doctor Ewing's summary, as quoted above, bears out the logic of Handley's investigations. Mr. Handley's clear vision of the pathology from the surgical point of view brings to our attention very forcibly how inadequate is the so-called radical operation as advocated by Willy Meyer, Rodman or Halsted. If it were only that cancer of the breast disseminated itself along lines which the radical operation can eliminate, one would be more satisfied with the possibilities of such an operation. Too often one is chagrined, after a period of one to ten years, to find dissemination of the original tumor appearing along the second, third and fourth intercostal spaces, near the sternum, or to find mediastinal and pleural involvement, or widespread or isolated bone metastases. Mr. Handley's

point is well taken in the technic of applying radium after radical operation in trying to eradicate the possible metastases to the anterior mediastinum. It has been my misfortune to see recurrences in this locality in numerous instances, appearing after years, some as late as seven, eight and nine years; as well as to see metastases in the supraclavicular lymph nodes, the mediastinum or the bones, on a few occasions thirteen, fifteen and twenty years after the original operation.

After my experience with cancer in general I am more and more inclined to believe that the word "cure," as applied to malignant disease, should be eliminated from the literature and the words "clinically well" be substituted.<sup>10</sup> The value of any therapy should be judged purely on the basis of comfort to the individual and the prolongation of life, even though the disease has not been eliminated from a pathological point of view. Whether this result

TABLE I

*Results of Operation in Carcinoma of the Breast without Irradiation and with Irradiation*  
(This is part of a table which appeared in a recent article by Pfahler and Parry<sup>11</sup>)

| Author                      | Without gland involvement                  |   | With gland involvement                     |   |
|-----------------------------|--|---|--|---|
|                             | Operation without irradiation<br>Per cent. | Operation with irradiation<br>Per cent. | Operation without irradiation<br>Per cent. | Operation with irradiation<br>Per cent. |
| König .....                 | 100  |   | 39   |   |
| Bloodgood .....             | 70   |   | 20   |   |
| Lee .....                   |  |   | 15   |   |
| Finisterer .....            |  |   | 4.3  |   |
| Doderlein .....             | 46   | 48                                      | 5  | 20                                      |
| Doderlein (completed) ..... |  | 80                                      |  | 36                                      |
| Wintz .....                 |  | 77                                      |  |   |
| Schmitz .....               |  | 64                                      |  | 42                                      |
| Perthes .....               |  |   | 25   |   |
| Anschutz .....              | 100  | 100                                     | 31   | 42                                      |
| Harrington .....            | 70.5                                       | 66.2                                    | 22.8                                       | 22.3                                    |
| Pfahler and Parry .....     |  | 89                                      |  | 47                                      |
| Schreiner .....             |  | 65                                      |  | 23                                      |

can be obtained by a given procedure or by a combination of procedures is of paramount importance. I believe that conservatism in surgery, together with radiation and other medicaments, may be the means to this end.

It should be our earnest endeavor to establish the limits of surgery as a possibility of eradicating cancer of the breast. The greatest discrepancies are seen in the statistical reports of competent observers,<sup>11</sup> Table I. Doctors Steinthal, Lee,<sup>12</sup> and Schmitz,<sup>13</sup> together with others, have tried to establish clinical groupings so that the results of cases reported in the literature can be better estimated. If all should decide on a grouping and classify their cases accordingly the statistics of five years hence would be more accurate and of the greatest value.

With this thought in mind I have separated these cases into primary carcinoma of the breast and post-operative recurrent carcinoma of the breast.

## RESULTS OF BREAST CANCER TREATMENT

The *primary cases* are divided into three groups. Group I consists of those cases in which the growth is confined to the breast and having no metastases, as evidenced by clinical and radiographic examinations, as well as, in the operative cases, by histological examination. In Group II are all carcinomas of the breast with definite metastases in the axilla, or ulceration of the breast which is fixed to the pectoral muscle, and showing without doubt involvement of the skin lymphatics. In Group III are the tumors of the breast, with or without axillary involvement, but with definite widespread metastases, as in the supraclavicular region, mediastinal or disseminated metastases. The *recurring carcinomas* of the breast are divided, as accurately as possible, into two groups. In Group I are those with local recurrence only; in Group II those with or without local recurrence but with disseminated metastases.

There were 480 cases of carcinoma of the breast admitted to the State Institute for the Study of Malignant Disease from 1914 to 1925. Of these 480 cases 283 were *primary* and were divided as follows: In Group I were seventy-one cases, fifty-two of which were treated by radical operation and

TABLE II  
*Showing Age Incidence at the Time of Admission*

|                        | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70-79 | 80-89 | 90-99 | Total |
|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Primary Group I....    | —     | 5     | 23    | 23    | 11    | 7     | 2     | —     | 71    |
| Primary Group II....   | 3     | 10    | 24    | 38    | 36    | 16    | 5     | —     | 132   |
| Primary Group III....  | —     | 6     | 13    | 25    | 20    | 12    | 3     | 1     | 80    |
| Recurring Group I....  | —     | 3     | 9     | 13    | 5     | 1     | —     | —     | 31    |
| Recurring Group II.... | 2     | 17    | 57    | 55    | 29    | 6     | —     | —     | 166   |
| Total.....             | 5     | 41    | 126   | 154   | 101   | 42    | 10    | 1     | 480   |

radiation, and nineteen treated by radiation alone. In Group II there were 132 cases, fifty-three of which were treated by radical operation and radiation, and seventy-nine by radiation alone. Most of these seventy-nine cases were, for one or more reasons, considered *not* suitable for operation. In Group III there were eighty cases. These were definitely inoperable and were treated by radiation alone. Of the 480 cases 197 were *recurrences*. These were divided as follows: In Group I, thirty-one cases with local recurrence only, treated by radiation alone, and 166 cases in Group II, local recurrence and disseminated metastases, which were treated by radiation alone.

The age incidence is depicted in Table II. The youngest patient was twenty-four, the oldest ninety years of age. Fifty-eight per cent. were between forty and sixty years old. These 480 patients were females, 388 of them being married, and ninety-two single. The disease was primary in the right breast in 214 cases, in the left breast in 231 cases; in thirty-five instances both breasts were involved, twenty-one of these being post-operative, recurring cases of Group II. A history of cancer in the family was reported by 110 of these women. The blood Wassermann reaction was positive in thirty-eight of these patients. Eighty-nine of these women gave a history of injury,

either in the form of a blow, a kick, fall or bruise, which they thought might have contributed to, or been the cause of, their trouble. Sixty-four per cent. of these patients gave a history of less than one year's duration at the time of admission, 77 per cent. of less than two years' duration. One hundred forty-three of these women had never been pregnant, the other 337 gave a history of from one to nine pregnancies.

*Treatment.*—Prior to 1920 these patients were treated with low voltage X-rays in divided doses,  $2\frac{1}{2}$  millimetres aluminum filter, 100,000 volts, 5 milliamperes, time factors varying from five to fifteen minutes at 20 to 30 centimetres' distance. Treatment was repeated sometimes at one-week intervals or two-week intervals over a period of one to three years, with intervals of rest depending on the condition of the skin.

From 1920 to 1925 the patients were treated by means of high voltage X-rays with varying technic as to distance and number of fields applied. During the years 1920, 1921 and 1922, cross-firing and massive doses were tried and resulted in much depression, X-ray sickness, and on the whole did not seem to justify the procedure that was then carried out. From 1923 to 1925 divided high-voltage X-rays were used which seemed more beneficial to the patients. The method was to divide a known quantity of X-rays over a period of a week to twelve days, allowing for the time elapsed between treatments; the desire being to administer from 120 to 150 per cent. on the skin. The factors of high-voltage X-rays were: 200,000 volts, 8 to 30 milliamperes, 0.5 millimetre copper, 1 millimetre aluminum filter, size of field 10 by 15 up to 20 by 20 centimetres, distance 40 to 50 centimetres, time factor depending on milliamperage and distance.

In some cases the implantation of radium emanation in glass seeds was resorted to. In a few cases radium packs were substituted for high-voltage X-rays, the factors being 6 centimetres' distance, 2 millimetres of brass, 1 millimetre of aluminum, 1 centimetre of rubber, for 6,000 to 8,000 millicurie hours per field.

In the cases which were operated, the radical operation according to the method of Willy Meyer was carried out.

#### RESULTS OF TREATMENT

480 cases treated. 283 *primary cases*. 52 cases in Group I were treated by *radical operation* and *radiation*. 4 of these died of intercurrent disease, having been clinically well one year, one year, three months, one year, six months, and for two years, seven months, respectively. 2 were lost trace of. 1 had been clinically well four years, the other one had a recurrence and was lost trace of in less than a year. 46 cases were available for study. 35 of these lived for from five to sixteen years from the time of treatment. 30 of the 46 cases, or 65 per cent., have been clinically well for five years or more. 1 has lived eight years. She was clinically well four years, ten months, when there was a recurrence in the scar which has healed twice since with radiation (for one year each time). Now the scar is thickened and adherent to the chest wall but she is feeling well. 1 died eight years after treatment. She had been clinically well two years, eight months following treatment when there was a recurrence in the axillary scar which responded to radiation and she was

## RESULTS OF BREAST CANCER TREATMENT

again well for two years, four months when she developed spinal and mediastinal metastases which caused her death, there being no evidence of recurrence externally. 1 died five years after treatment. She developed mediastinal metastases two years, three months after treatment, the operative site remaining well at the time of death. 1 died in five years. She had been clinically well four years when metastases developed in the supraclavicular region, thyroid and sternomastoid muscle. 1 is alive five years after treatment. Two years after treatment she developed mediastinal nodes, followed by glandular involvement of both hila and four years after treatment there was metastasis in the supraclavicular region. The operative site remains well.

11 patients died in less than five years. In 8 the operative site remained well but metastases developed and they died as follows: 1 in nine months from mediastinal metastases; 4 in from one to two years, 1 from liver metastases, 1 from metastases to the brain and mediastinum; 1 from metastases to the supraclavicular region and liver, 1 from metastases in pancreas and liver. 1 in from two to three years from liver metastases. 2 in from three to four years; 1 from carcinoma of the other breast and metastases in the supraclavicular region and mediastinum, 1 from metastases in the liver. 3 patients had local recurrence and metastases and died: 2 in from one to two years from recurrence and general metastases; 1 in four years nine months. She had been clinically well one year, two months, when there was a recurrence over the fourth rib which gradually extended over the chest and into the mediastinum.

19 cases in Group I were treated by *radiation only*. 3 died of intercurrent disease in one year, two years, and in two years, seven months, respectively, 2 being clinically well, the other much improved. 2 were lost trace of in less than a year. 14 cases available for study. 6 of these lived for five years or more. 4 of the 14 cases, or 28 per cent., have been clinically well five years or more. 1 is living eight years, eight months from the time of admission. She has had supraclavicular and axillary nodes for the past two years. 1 died six years from the time of admission. She had been clinically well two years, five months when there was a recurrence locally, followed by definite mediastinal involvement four years after admission. 8 patients died in less than five years: 1 in less than one year, unimproved; 2 in from one to two years, 1 unimproved, the other from carcinoma of the stomach, the breast lesion having healed; 2 in from two to three years, unimproved; 1 in from three to four years, having been clinically well one year, nine months when there was local recurrence; 2 in from four to five years, 1 had been clinically well one year when there was local recurrence, 1 died from mediastinal and spinal metastases, the breast having never entirely healed.

Nine of the 19 cases, or 47 per cent., showed marked improvement, which, however, was not lasting.

53 cases in Group II were treated by *radical operation and radiation*. 4 died of intercurrent disease, 3 having been clinically well six months, ten months and two and a half years, respectively; 1 in one and a half years, after recurrence. 6 were lost trace of in less than a year. 3 had had recurrence. 3 were clinically well when last seen. 43 cases available for study. 15 lived for from five to ten years. 10 of the 43, or 23 per cent., have been clinically well five years or more. 1 was clinically well for one year when there was a local recurrence and she died in five years. 1 was clinically well for four years when there was a local recurrence and distant metastases developed and they died as follows: 2 in less than one year, 1 from five years. 1 was clinically well two years when there were definite skin metastases which became progressively worse and she died from mediastinal metastases five years from the time of admission. 1 was clinically well four years, two months when there was local recurrence. She died six years, nine months from the time of admission. 1 is living eight years after admission. She developed a recurrent

- node in the axilla three months after treatment, and a recurrence in the scar in the chest four years, three months after treatment.
- 28 patients died in less than five years. In 5 the operative site remained well but metastases developed and they died as follows: 2 in less than one year, 1 from abdominal metastases, 1 from liver and spinal metastases; 2 in from two to three years, 1 from mediastinal metastases, 1 from abdominal metastases; 1 in from four to five years, having been clinically well three years, six months when she developed spinal metastases.
- 23 patients had local recurrence and metastases and died as follows: 6 in less than one year, 8 in from one to two years, 3 in from two to three years, 4 in from three to four years, 2 in from four to five years. One of these had been clinically well one year, seven months when there was a recurrent node in the axilla, definite recurrence in the scar not appearing until four years, five months after treatment.
- 79 cases in Group II were treated by *radiation only*: 7 were unimproved and lost trace of in from a few months to three years. 3 died from intercurrent disease, all improved, 2 in three months, 1 in one year, eight months. 69 cases were available for study. 10 have lived for from five to nine years. 1 of the 69 cases, or 1.4 per cent., has been clinically well five years. 1 was clinically well three years when skin nodules appeared and the condition has remained the same. 1 died in five years, five months from the disease and metastases. 1 died in five years from intercurrent disease. There had been no clinical evidence of the disease for a period of four months prior to death. 1 died in six years from the disease. 1 died in six years, four months from mediastinal metastases; local improvement. 1 was clinically well one year, eight months when there was local recurrence and she died six years, seven months from the time of admission. 1 was clinically well two years when there was local recurrence and she died in seven years from the time of admission. 1 was clinically well one year when there was mediastinal involvement, followed in two years by local recurrence. She feels well eight years after admission; there is a hard sclerosed tumor in the breast. 1 was clinically well three years, eight months when there was local recurrence and metastases over the whole chest. She died eight years, two months from the time of admission.
- 59 patients died in less than five years; 17 in less than one year. In one the breast was healed and she died from carcinoma of the uterus. 14 died in from one to two years. 12 were unimproved. 2 had been clinically well eight months and one year, eight months, respectively, when there was local recurrence. 9 died in from two to three years. 7 were unimproved. 1 died from metastases in the liver and uterus, having been clinically well two years. 1 died from distant metastases, the node in the axilla had persisted but the breast healed. 13 died in from three to four years. 12 had palliation only. 1 was clinically well three years when there was local recurrence as well as metastases. 6 died in from four to five years; all had had good palliation.
- 80 cases in Group III were treated by *radiation only*: 7 were lost trace of. 4 in less than a year, 2 in from one to two years, 1 in from four to five years. 73 cases available for study. 2 patients are living over five years: 1 for six years from the time of admission, she has had marked regression in the primary tumor and in the metastases in the supraclavicular and axillary regions, mediastinal metastases still present; 1 for seven years, she had supraclavicular nodes on admission and has been clinically well for the past three years. 71 patients died in less than five years as follows: 33 in less than one year; 20 in from one to two years; 6 in from two to three years; 6 in from three to four years, one of these had been clinically well three years when there was local recurrence and metastases in the liver; 6 died in from four to five years, one of these had lung involvement at the time of admission, the breast lesion had been healed for two years prior to death.

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197 recurring cases. 31 cases in Group I were treated by *radiation only*: 2 died of intercurrent disease, having been clinically well one and a half years and two years, respectively. 3 were lost trace of in less than one year. 26 cases available for study. All died in less than five years from the recurrence and metastases as follows: 11 in less than one year, 9 in from one to two years (2 of these had seemed clinically well for a few months), 4 in from two to three years, 2 in from four to five years. One of these had been clinically well for two years when there was local recurrence as well as metastases.

166 cases in Group II were treated by *radiation only*: 29 were lost trace of, 28 in less than one year, only one having shown improvement. 1 in two years. 137 cases were available for study: 6 of these lived five to seven years: 1 has been alive for five years from the time of admission. She had mediastinal metastases and nodes in the scar at the time of admission; these healed with X-ray treatment for nine months. 1 has been alive for five years. She had supraclavicular nodes at the time of admission which were held in check by radiation. She developed mediastinal metastases two years after admission. 3 died in from six to seven years, 1 showed marked regression of the local recurrence, palliation lasting up to seven years. 1 had marked palliation for over three years, 1 died from mediastinal metastases, there having been no local recurrence for three years prior to death; 1 patient is living seven years, three months, from the time of admission. There has been marked regression of the metastases in the supraclavicular region, although we are suspicious that there is now mediastinal involvement. 82 died in less than one year. 37 in from one to two years. 6 in from two to three years (one of these had marked palliation). 6 in from three to four years (one showed marked regression of the metastases, another was well externally for three years when she died from the mediastinal involvement which she had at the time of admission).

### SUMMARY

The *absolute statistics* of the 283 primary cases show that forty-five, or 16 per cent., have been clinically well for five years or more; that thirty, or 58 per cent., of the fifty-two primary Group I cases, treated by operation and radiation, have been clinically well five years or more; that four, or 21 per cent., of the nineteen primary Group I cases, treated by radiation only, have been clinically well five years or more; that ten, or 19 per cent., of the fifty-three primary Group II cases, treated by operation and radiation, have been clinically well five years or more; that one, or 1.2 per cent., of the seventy-nine primary Group II cases, treated by radiation only, has been clinically well five years or more. No case in primary Group III, treated by radiation only, has been clinically well five years. No case in the recurrent Group I, or recurrent Group II, treated by radiation only, has been clinically well for five years.

Statistics based on patients available for study:

*Primary Group I.*—Of forty-six cases treated by operation and radiation, thirty, or 65 per cent., have remained clinically well for five years or more. Of fourteen cases treated by radiation only four, or 28 per cent., have remained clinically well for five years or more.

*Primary Group II.*—Of forty-three cases treated by operation and radiation, ten, or 23 per cent., have remained clinically well for five years or more.



Of sixty-nine cases treated by radiation only, one, or 1.4 per cent., has remained clinically well five years or more.

*Primary Group III.*—Palliations are shown in this group of seventy-three cases in the longevity of the patients. From the time of admission: 2½ per cent. lived five years or more; 8 per cent. died in from four to five years; 8 per cent. died in from three to four years; 8 per cent. died in from two to three years; 27 per cent. died in from one to two years; 45 per cent. died in less than one year.

*Recurrent Group I.*—Of twenty-six patients, treated by radiation only, from the time of admission: 7.6 per cent. died in from four to five years; 15.3 per cent. died in from two to three years; 34.6 per cent. died in from one to two years; 42.3 per cent. died in less than one year.

*Recurrent Group II.*—Of 137 patients, treated by radiation only, from the time of admission: 4.3 per cent. lived over five years; 4.3 per cent. died in from three to four years; 4.3 per cent. died in from two to three years; 27.0 per cent. died in from one to two years; 59.8 per cent. died in less than one year.

#### CONCLUSIONS

1. In primary operable Group I cases, treated by radical operation and radiation, 65 per cent. of those available for study were clinically well five years or more; of those treated by radiation alone, 28 per cent. remained clinically well five years or more.

2. In primary Group II cases, treated by radical operation and radiation, 23 per cent. have remained clinically well five years or more; of those treated by radiation alone (which were inoperable) 1.2 per cent. remained clinically well five years or more.

3. The primary Group III cases, treated by radiation alone, have yielded palliations only.

4. The recurring cases, Group I and Group II, treated by radiation alone, have yielded palliations only.

5. I am convinced that irradiation is of distinct value in the retardation of the growth and the amelioration of suffering and in the prolongation of life.

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# METASTASES TO THE SKELETON, BRAIN AND SPINAL CORD FROM CANCER OF THE BREAST AND THE EFFECT OF RADIOTHERAPY

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THE clinical course and response to therapy of metastases from cancer of the breast may best be studied in patients whose histories are known from the time of discovery of the tumor to the time of death. Patients alive when they are investigated or those dying accidentally or from intercurrent diseases, illustrate only single chapters in the life history of the cancer and do not give a true picture of the disease as a whole.

The greater number of patients with cancer of the breast admitted to the Radiotherapeutic and Surgical Services of the Montefiore Hospital of New York during the past ten years, reached the hospital in the terminal stage of the disease. They died shortly after, either in the hospital or at home while under direct or indirect supervision of the medical staff of these services. The clinical course of the earlier phases of the disease had to be reconstructed in most cases from the history as given by the patient or from records of other hospitals. Through the coöperation of the departments of pathology of Montefiore Hospital and several other hospitals, histological studies on the original tumor and its metastases were made possible in nearly four-fifths of the cases.\*

*Material.*—One hundred and sixty-eight cases of carcinoma of the breast with metastases to various parts of the body were studied from the time of the discovery of the tumor to the time of death. Nearly half (eighty-one cases) had skeletal metastases, proven röntgenographically or at autopsy. More than half of these had involvement of the lumbosacral spine and about one third of the skull. Of the latter, more than half gave neurologic signs

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of brain involvement and of the former, thirteen cases were thought to have spinal-cord metastases. No cases of spinal-cord involvement were observed in the absence of evidence of the disease in the lumbosacral spine. It is doubtful whether true metastases to the spinal cord occurred, in as much as autopsy of four of the thirteen showed, in three only compression of and in one an extension into the cord. A similar problem arose with regard to brain involvement: in nine autopsies, extension from the calvarium to the dura was found in one, extension from the calvarium through the dura to the brain in three, and multiple metastases apparently spread by the blood-stream in five. It can thus be seen that clinical differentiation of compression, extension and true metastases from carcinoma of the breast in the central nervous system is difficult if not impossible. Of the eighty-five cases of metastases to the skeleton and central nervous system, sixty-seven were verified histologically; thirty-two of these were examined post-mortem. Sixty cases of the eighty-five could be grouped according to histological evidence of malignancy, into Grade I, or least malignant, Grade II, or moderately malignant, and Grade III or most malignant. Of the eighty-five cases nearly 66 per cent. (fifty-six cases) had radical mastectomies; 15 per cent. (thirteen cases) were not operated upon; 8 per cent. (seven cases) had simple mastectomies, and 6 per cent. (five cases) had only biopsies. Many cases were so far advanced when admitted to the Montefiore Hospital that radiotherapy was withheld, or one X-ray treatment given for psychological reasons. These latter cases have not been used in evaluating the efficiency of radiotherapy.

*Definitions.*—The term of life of the patient, from the time of the discovery of the primary tumor to death, was divided into two periods. The last third was designated as terminal in contrast to the earlier two-thirds or pre-terminal. An exception was made in the case of patients who lived over three years. In these, the last year of life was looked upon as the terminal stage. It was found that at least 55 per cent. of the cases of skeletal metastases occurred during the pre-terminal period of the disease, and that survival in this group after the appearance of clinical evidence of skeletal metastases varied from a few months in fulminating cases to four and two-thirds years in the slowly advancing carcinomas.

Our criterion for clinical evidence of skeletal metastases was pain or tenderness localized in a part of a bone which later showed the typical röntgenographic picture of metastasis, or in which cancer was found at autopsy. All of the cases quoted in this paper as skeletal metastases have been thus verified. The clinical diagnosis of brain and cord involvement was based on symptoms of increased intracranial pressure or neurologic signs of localized cerebral, cerebellar, brain stem or cord involvement. The difficulty of differentiating between compression, extension and true metastases in this connection has already been mentioned. Clinical diagnosis of pulmonary and pleural metastases was made on subjective symptoms or physical signs of a process in the lungs which could not be explained on other grounds, and in which later, röntgenographic or post-mortem evidence of cancer was found.

Under skin metastases, were included typical cutaneous and subcutaneous nodules in or near the operative scar, or related to a carcinomatous ulcer. Direct extension from a broken-down carcinomatous ulcer of the skin was excluded, as it was felt that this was not a true metastasis. In spite of probable errors and the incompleteness of individual case histories, it is believed that the sum total of information gathered allows certain general conclusions which hold true for the average case of carcinoma of the breast with metastases to the skeletal and central nervous systems.

*Sex, Age, Location of Primary Tumor.*—Of the eighty-one cases with skeletal metastases, eighty were in women and one was in a man.

The age of the patients when the tumor was first noted, varied from twenty-two to seventy-five years. As seen from Table I the greatest number of cases occurred between the ages of forty and fifty years. A definite relationship between age and duration of life following the discovery of the tumor could not be established. Several of our youngest patients were among those who lived for a long period while some of the oldest patients died soon after the discovery of the tumor.

TABLE I  
*Age When Tumor Was Noted—81 Cases*

| Age Groups    | Per cent.<br>of cases |
|---------------|-----------------------|
| Under 30..... | 5                     |
| 30-40.....    | 30                    |
| 40-50.....    | 37                    |
| 50-60.....    | 19                    |
| 60-70.....    | 8                     |
| Above 70..... | 1                     |

The primary tumor arose in the right breast in forty-three cases and in the left breast in thirty-eight cases. Data giving more exact localization of the tumor in the breast were too incomplete to be of much value. Information regarding clinical or microscopical involvement of axillary lymph-nodes was frequently so unsatisfactory that it was decided to leave this factor also out of consideration.

*Anatomical Distribution of Skeletal Metastases.*—Among the eighty-one patients there were only 16 per cent. (thirteen cases) that apparently had metastases to the skeleton alone. In the rest, *i.e.* 84 per cent. (sixty-eight cases) skeletal invasion was associated with metastases to one or several of the other body systems. The distribution of these metastases in eighty-one cases was as follows: lungs 52 per cent. (forty-two cases), skin 36 per cent. (twenty-nine cases), brain 21 per cent. (seventeen cases), spinal cord 16 per cent. (thirteen cases).

Most of the skeletal metastases were multiple. Of the eighty-one cases only fourteen showed involvement of a single bone, and even in these it may be questioned whether some other metastasis was not overlooked.

The regional distribution of the metastases was investigated, first as to

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general distribution, and secondly as to the site of the first localization. The latter study probably gives a truer picture of the predilection of the metastatic process for certain bones especially if the pre-terminal cases are considered separately.

TABLE II  
*Anatomical Distribution in 81 Cases of Skeletal Metastases\**

| General localization | Per cent. | No. of cases | Specific localization | Per cent. | No. of cases | Homolateral†<br>Heterolateral<br>Bilateral                |
|----------------------|-----------|--------------|-----------------------|-----------|--------------|---|
| Pelvis.....          | 62        | 51           | Ischium..             | 37        | 19           |   |
|                      |           |              | Ilium....             | 58        | 30           |   |
|                      |           |              | Pubis....             | 56        | 29           |   |
| Spine.....           | 59        | 48           | Cervical .            | 13        | 8            |   |
|                      |           |              | Dorsal...             | 40        | 24           |   |
|                      |           |              | Lumbar..              | 57        | 34           |   |
|                      |           |              | Sacral....            | 38        | 23           |   |
| Femur.....           | 54        | 44           |                       |           |              | Bilateral..... 31<br>Heterolateral.. 8<br>Homolateral.. 5 |
| Ribs.....            | 39        | 32           |                       |           |              | Bilateral..... 20<br>Heterolateral.. 5<br>Homolateral.. 7 |
| Skull.....           | 35        | 29           |                       |           |              |   |
| Humerus.....         | 27        | 22           |                       |           |              | Bilateral..... 11<br>Heterolateral.. 5<br>Homolateral.. 6 |
| Scapula.....         | 16        | 13           |                       |           |              | Bilateral..... 8<br>Heterolateral.. 4<br>Homolateral.. 1  |
| Clavicle.....        | 14        | 12           |                       |           |              | Homolateral.. 1<br>Bilateral..... 5<br>Heterolateral.. 6  |
| Tibia.....           | 3         | 3            |                       |           |              | Homolateral.. 2<br>Heterolateral.. 1                      |
| Sternum.....         | 1         | 1            |                       |           |              |   |
| Radius.....          | 1         | 1            |                       |           |              |   |
| Ulna.....            | 1         | 1            |                       |           |              |   |
| Hands.....           | 1         | 1            |                       |           |              |   |
| Fibula.....          | 1         | 1            |                       |           |              |   |
| Bones of Feet.....   | 1         | 1            |                       |           |              |   |

NOTE.—\* Most of the cases had multiple metastases, so that the same case may appear under several headings. A clearer picture of the relative frequency may be obtained from Table III.  
† "Homolateral" designates occurrence on the same side as the primary growth in the breast: e.g. right breast and right femur; "Heterolateral" on the opposite side.

Of the forty-five cases of skeletal metastases occurring in the pre-terminal stage the skeleton was the primary localization in 82 per cent. (thirty-nine cases). In only six cases did röntgenographic or clinical evidence of other metastases precede skeletal invasion; in three these were pulmonary and in three cutaneous metastases. The metastases however did not remain localized

TABLE III

*The First Site of Involvement as Suggested by Pain and Later Confirmed Röntgenographically.*  
75 Cases

|                         | Per cent. | No. Cases |
|-------------------------|-----------|-----------|
| Sacro-lumbar spine..... | 37        | 28        |
| Femur.....              | 16        | 12        |
| Pelvis.....             | 14        | 11        |
| Skull.....              | 13        | 10        |
| Dorsal spine.....       | 5         | 4         |
| Ribs.....               | 5         | 4         |
| Humerus.....            | 4         | 3         |
| Scapula.....            | 2         | 2         |
| Clavicle.....           | 1         | 1         |
| Tibia.....              | 1         | 1         |

to the skeleton. In 80 per cent. (thirty-six cases) they were complicated by metastases to other parts of the body. In ten the skeletal metastases were followed by pulmonary and in ten others by cutaneous invasion. The relationship between the time of onset of skeletal and other metastases could not be determined in the remaining cases. The regional distribution of the first localization in the forty-five cases occurring in the pre-terminal stage is given in Table IV.

TABLE IV

*First Localization in the Skeleton of Cases in the Pre-Terminal Stage, 45 Cases*

| Region                  | Per cent. | No. of Cases                          |
|-------------------------|-----------|---------------------------------------|
| Lumbo-sacral spine..... | 39        | 17                                    |
| Femur.....              | 18        | 8 {heterolateral, 7<br>homolateral, 1 |
| Pelvis.....             | 16        | 7                                     |
| Skull.....              | 8         | 4                                     |
| Dorsal spine.....       | 7         | 3                                     |
| Ribs.....               | 4         | 2                                     |
| Scapula.....            | 4         | 2 {homolateral, 1<br>heterolateral, 1 |
| Humerus.....            | 2         | 1 heterolateral                       |

The anatomical distribution of metastases as given in Table IV corresponds to the finding of Lee,<sup>21</sup> Semken,<sup>30</sup> and others, and differs somewhat from that quoted by Handley,<sup>13</sup> and more recently by Carnett and Howell.<sup>3</sup> While the figures on the frequency of involvement of the sternum and ribs quoted by Handley are probably nearer the truth than those given here, metastases to the lumbosacral spine, pelvis, and femur, surely occur more often than it would appear from the tables of this author. The discrepancy may be due to the fact that the criterion for localization of skeletal metastases in this series was pain and later a positive röntgenogram, whereas Handley's statistics are based on autopsy findings. It is well known that röntgenographs of metastases in the sternum and the adjacent portion of the ribs are rarely satisfactory.

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*Histological Grading of Malignancy and Its Bearing on the Survival Period Following Discovery of the Tumor, the Metastases, and the Time Interval between These.*—The microscopic structure of the primary tumor, or the metastases or both were investigated and an attempt was made in fifty-seven cases of skeletal metastases to grade the tumor according to the histological evidence of malignancy without reference to the clinical history. Variation in size and staining qualities of the cells and nuclei, frequency of mitotic figures, secretion vacuoles, glandular differentiation, connective tissue reaction, round-cell infiltration, and necrosis were studied. The order of importance of these factors in determining the degree of malignancy, is that just given. Grouping into Grade I and III was comparatively easy. Grouping of cases into Grade II on the other hand was difficult, as the histological characteristics in many cases approached either Grade I or III. This is illustrated in the following case.

B.G., with a primary inoperable carcinoma of the left breast, had a biopsy done and three years later died of broncho-pneumonia. The histological picture of the original tumor showed extreme variation in the size and staining qualities of cells and nuclei, two to three mitotic figures per high power microscopic field, no secretion vacuoles or attempt at glandular differentiation. Specimens obtained at post-mortem examination from skull, dura, brain and adrenals, on the other hand, showed slight to moderate variation in the size and staining qualities of cells, practically no mitotic figures, no secretion vacuoles, but a slight attempt at glandular differentiation. Our classification based on sections of the original tumor would have been Grade III, on sections from the autopsy material, Grade I. After seeing both we grouped the case as belonging to Grade II.

Of the fifty-seven cases twenty-six were thus classed in Grade I, twenty-six in Grade II, and five in Grade III. While inaccuracies in grading occurred, the general clinical value of this histological grading is supported by a study of the survival period after the discovery of the tumor as illustrated in Table V. It is interesting to note that five cases of Grade I with marked

TABLE V

*Survival Period According to Histological Grading, 57 Cases*

| Grade    | No. of Cases | Average duration of life in months |
|----------|--------------|------------------------------------|
| I.....   | 26           | 50.2                               |
| II.....  | 26           | 23.5                               |
| III..... | 5            | 17.3                               |

glandular differentiation had an average survival period of 71.1 months as compared to an average survival period of forty-five months for the twenty-one other cases which did not show this histologic characteristic.

Cases with marked connective tissue reaction (scirrhous cancer) showed somewhat increased survival periods for Class II and III, not for Class I. The significance of this finding may be questioned.

There were thirty-nine cases in which a radical amputation of the breast was done and six non-operated cases which could be graded according to the histological evidence of malignancy. The survival period varied with the histological grading and appeared to be somewhat shorter in the non-operated



TABLE VI

*Survival Period in Cases with Marked Connective Tissue Reaction, 16 Cases*

| Group    | No. of Cases | Survival period<br>in months |
|----------|--------------|------------------------------|
| I.....   | 6            | 49.4                         |
| II.....  | 8            | 32.3                         |
| III..... | 2            | 20                           |

series. However, definite conclusions cannot be drawn on this last question on account of the marked numerical divergence of the two series. It might be interesting to mention, that the only three patients of the radically operated Grade I group that survived a year or less after the tumor was noted, were patients who showed pain and tenderness in bones before the operation, and post-operatively showed röntgenographic evidences of skeletal metastases. Whether this is a coincidence in patients operated upon when they were nearing their terminal stage, or whether the operative interference so lowered their resistance as to accelerate the approach of death offers interesting material for speculation.

TABLE VII

*Duration of Life Arranged According to Histological Grading—46 Cases*

| Group    | Cases with radical amputation<br>of the breast |  | Non-operated cases |  |
|----------|--|--|--------------------|--|
|          | No. of<br>cases                                | Survival period<br>discovery of tumor<br>to death (months) | No. of<br>cases    | Survival period<br>discovery of tumor<br>to death (months) |
| I.....   | 22   | 53.6   | 1                  | 30   |
| II.....  | 14   | 41.2   | 4                  | 27.7   |
| III..... | 3  | 20   | 2                  | 13.5   |

The influence on the survival period of the pre-operative duration of a palpable tumor in cases subjected to radical amputation of the breast was studied, but no definite conclusions could be arrived at, perhaps on account of lack of sufficient material. It seemed however that patients in whom the rate of growth of the tumor was slow<sup>23</sup> and who therefore visited the surgeon and were operated upon late did better than those in whom the rate of growth was rapid, caused discomfort and who were operated upon earlier. This in no way affects the advisability of early operation, but is the probable explanation of this unexpected finding. For instance, in three Grade III cases a radical mastectomy had been performed three months after the tumor was noted. The average survival period in these was only seventeen and one-third months. On the other hand in four cases of Grade I in whom the tumor had been noted for more than a year prior to the time of mastectomy the survival period was 47.6 months.

Our data was insufficient to form conclusions as to the possible influence of castration on the occurrence of skeletal metastases.

The time interval between the discovery of the primary breast tumor and

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TABLE VIII

*Interval Between Discovery of Tumor and Onset of Skeletal Metastases—43 Cases*

| Group    | Radically operated cases |   | Non-operated cases |   |
|----------|--------------------------|---|--------------------|---|
|          | No. of cases             | Interval between discovery of tumor and onset of metast. (months) | No. of cases       | Interval between discovery of tumor and onset of metast. (months) |
| I.....   | 19                       | 46.5  | 1                  | 29  |
| II.....  | 14                       | 29.1  | 4                  | 21.1  |
| III..... | 3                        | 10  | 2                  | 6   |

the onset of symptoms of skeletal metastases as seen from Table VIII also seem to depend greatly on the histological grading of the tumor.

Survival after the onset of skeletal metastases varied from three months to four years and eight months. The combined terminal and pre-terminal, and then the latter alone were studied and graded histologically in Tables IX and X.

TABLE IX

*Survival After Onset of Skeletal Metastases, 50 Cases*

| Grade    | No. of Cases | Survival period in months |
|----------|--------------|---------------------------|
| I.....   | 23           | 15.1                      |
| II.....  | 22           | 8                         |
| III..... | 5            | 9                         |

TABLE X

*Survival of Pre-Terminal Cases After Onset of Skeletal Metastases, 32 Cases*

| Grade    | No. of Cases | Survival period |
|----------|--------------|-----------------|
| I.....   | 15           | 19.7            |
| II.....  | 13           | 16.2            |
| III..... | 4            | 10              |

The slightly longer survival period in the pre-terminal group as compared with the general group is naturally what one would expect.

*Clinical Symptomatology of Metastases to the Skeleton.*—Pain<sup>11, 24</sup> and less frequently bony tenderness on direct pressure or percussion are usually the first symptoms of invasion of the skeletal system by metastases from cancer of the breast. In 75 per cent. *i.e.*, sixty-one of the eighty-one cases, attention was drawn to the presence of bony metastases through the fact that the patient complained of localized pain. This was usually at the site of the metastases, occasionally, however, over the area of distribution of the nerve immediately adjacent to the metastases. In 17 per cent. (fourteen cases) pain occurred at about the same time as röntgenographic corroboration was obtained and in only 7 per cent. (six cases) were metastases discovered incidentally when röntgenographs were made as a routine measure, the patient not complaining of any pain. In nine cases it was possible to follow the gradual appearance of definite röntgenographic evidence of skeletal metastases in places where the patient complained of pain from one-half to twelve months

prior to positive röntgenograms. In these cases röntgenographs were made at frequent intervals until they became positive. In six of the cases the skeletal metastasis was the first point of localization; in three, involvement of other parts of the skeletal system had been diagnosed röntgenographically and attention to the new invasion was drawn by the patient's complaints. A table of the nine cases follows:

| Interval between onset of pain and positive Röntgenographs | Clinical symptoms   | Röntgenographs   |
|--|---|--|
| ½ mo.  | F. H.—Severe pain sternal end of left clavicle 18½ months after discovery of tumor.   | 18½ mos. P.T.* Clavicles negative.<br>19 mos. P.T. Path. fracture 2" from sternal end of left clavicle.  |
| 3½ mos.  | A. B.—When tumor discovered, pain in lumbar and sacral regions radiating anteriorly. Pain continued following operation 2 mos. later.   | 2 mos. P.T. Lumbar spine negative.<br>3½ mos. P.T. Slight narrowing of body of 1st L.V. Small area of bone absorption in left wing of sacrum.  |
| 3 mos.   | C. T.—14 mos. P.T. Pain and tenderness 2nd left rib anteriorly.   | 14 mos. P.T. Chest and shoulders negative.<br>19 mos. P.T. Metastases 6, 7th right ribs 7th left rib.<br>22 mos. P.T. Metastases in practically all the ribs.  |
| 5 mos.   | R. K.—7 mos. P.T. Pain in left hip and crest of ilium.<br>9 mos. P.T. Tenderness in lumbar spine and left hip.<br>12 mos. P.T. Pain in left hip radiating to ankles, right hip and also right shoulder. | 9 mos. P.T. Pelvis and upper third of femora negative.<br>12 mos. P.T. Small area of rarefaction in left pubic bone. Femora negative.<br>17 mos. P.T. Area of bone destruction and sclerosis in descending ramus of right ischium. Metastases in left os and descending ramus of left pubis. |
| 6 mos.   | H. F.—9 yrs. 9 mos. P.T. Pain right foot. Pain in right foot persisted.   | 9 yrs. 9 mos. P.T. Right foot negative.<br>10 yrs. 3 mos. P.T. Metastasis to right cuneiform bone.   |
| 7 mos.   | R. T.—16 mos. P.T. Severe pain in dorsal region.  | 16 mos. P.T. Dorsal region negative.<br>23 mos. P.T. Multiple metastases in dorsal vertebrae.  |
| 7 mos.   | S.—27 mos. P.O. Pain in both shoulders radiating down the arms. Pain persisted.   | 27 mos. P.O. Shoulders negative on numerous chest films taken before and following this date.<br>34 mos. P.O. Metastasis to head of right humerus.   |
| 8 mos.   | R. K.—34 mos. P.T. Pain right leg.<br>36 mos. P.T. Pain and tenderness right lower tibia.<br>38 mos. P.T. Marked tenderness over tibia.<br>42 mos. P.T. Swelling and tenderness right ankle.            | 34 mos. P.T. Right leg and foot negative.<br>37 mos. P.T. Right ankle and leg negative.<br>39 mos. P.T. Right tibia negative.<br>42 mos. P.T. Few areas of bone destruction lower end of right tibia and fibula; röntgenographic appearance suggestive of metastases.                        |

\* P.T. after discovery of tumor; P.O. after operation.

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| Interval between onset of pain and positive Röntgenographs | Clinical symptoms  | Röntgenographs  |
|--|--|---|
| 11 mos.  | C. T.—16 mos. P.T. Pain and tenderness both scapulæ.   | 16 mos. P.T. Shoulders negative.<br>19 and 22 mos. P.T. Chest X-rayed for ribs—negative.<br>28 mos. P.T. Multiple metastases in scapulæ.  |
| 12 mos.  | R. B.—16 mos. P.T. Onset of pain and bony tenderness right ribs.   | 10 to 16 mos. P.T. Röntgenographs of chest during this period were negative for rib metastases.<br>22 mos. P.T. Metastasis to 2nd right rib.  |
| 12 mos.  | R. S.—7 mos. P.T. Pain in back.<br>11 mos. P.T. Radical mastectomy. Pain in back persisted post-operatively.<br>18 mos. P.T. Pain in back became very severe and started to radiate down the thighs. | 11 mos. P.T. Lumbo-dorsal spine negative.<br>13½ mos. P.T. Pelvis negative.<br>19 mos. P.T. Extensive metastases to 4th and 5th lumbar vertebræ<br>21 mos. P.T. Metastases to all lumbar vertebræ and pelvis. |

Pain apparently is earliest and most pronounced where pressure due to natural body weight or muscular tension is greatest. Thus, for instance, pain due to invasion of the lumbar spine or sacro-iliac region is usually present early, whereas pain due to invasion of the vault of the skull is commonly not complained of until late in the course of this metastasis, when it has either reached a considerable size or is producing increased intra-cranial pressure. While pain and bony tenderness usually indicate the presence of skeletal metastases, this diagnosis can only be made on the basis of röntgenographic evidence or microscopical examination. Indirect symptoms of skeletal metastases such as cachexia and unusual blood findings such as mentioned by Piney<sup>27</sup> were not carefully studied in this series. It was found, however, that cachexia did not seem to be an important symptom except in the terminal stage of the disease.

*Röntgenographic Corroboration.*—Before the advent of recent improvements in röntgenographic technic<sup>2</sup> and the recognition of the frequency of skeletal metastases, many cases were missed. At present, however, many more metastases are recognized. The röntgenographic characteristics of skeletal metastases from cancer of the breast closely correspond to the pathological findings. The lesions may be circumscribed or diffusely infiltrating. They are generally of the osteoclastic type (77 per cent. in this series) and less frequently a mixture of osteoclastic and osteoblastic types with the one or the other predominating (23 per cent. in this series). In some cases the amount of new bone laid down is so great that the areas involved become very dense and röntgenographically give an almost ivory-like appearance. The extensive, infiltrating types of skeletal metastases are the ones most likely to show osteosclerosis. Small localized areas of bone sclerosis are

occasionally seen especially near the sacro-iliac joint. These areas may be benign, but require repeated röntgenographic check-up in order to avoid overlooking the development of early metastases. The same caution should be exercised in interpreting the significance of röntgenographic evidence of spondylitis. This may often mask an early metastasis.

*Pathological Fractures.*—Pathological fractures of one or more of the long or flat bones were encountered in 26 per cent. of the cases (twenty-one of eighty-one). They occurred only in the terminal stage of the disease. Fractures were observed in the femur (nine cases), humerus (nine cases), ribs (two cases), and clavicle (one case). The fractures of the ribs were probably much more numerous, but were missed on account of the difficulty of the röntgenographic diagnosis of rib involvement.

*Effect of Radiotherapy.*—In considering the possible benefits from radiotherapy in skeletal metastases it should be remembered that the greater number of patients were admitted to the Radiotherapy Department of Montefiore Hospital during the terminal stage of the disease. In only thirty-one of the eighty-one cases was it possible to evaluate the results of radiotherapy. The number of treated cases in each of the histological grades was insufficient to permit any definite conclusion on this question. The metastases were usually so widespread that only mild palliation was attempted. In three cases the metastases seemed to be localized to a single bone. Two of these improved in spite of the fact that they were in the terminal stage of the disease. In nineteen cases treated during the terminal stage of the disease, ten showed clinical improvement and nine remained unimproved. Of twelve cases treated in the pre-terminal stage, all were markedly improved by therapy. The duration of improvement varied from a few weeks to three years. It was manifested in relief of pain within twenty-four to forty-eight hours after the first X-ray treatment; and there was progressive improvement in many cases. The clinical improvement was at times striking. Thus we had two patients that were admitted as apparently hopeless and moribund, who were able to leave the hospital walking after they had received a series of X-ray treatments. They remained clinically well for twenty-seven and thirty-six months respectively. One of them, a milliner, was able to follow her regular occupation during a period of over three years.

Bone sclerosis following X-ray therapy occurred in fourteen of thirty-one cases. In ten this had not been present prior to irradiation, in four the metastases were osteoblastic before irradiation and the bone sclerosis was somewhat increased in density following the treatment. The dosage apparently was not the determining factor in producing the improvement. Most of the cases were treated with X-rays with the following factors: 200 KV, 0.5 millimetre copper filter, 50 centimetre target skin distance, and moderately sized fields. A few cases were treated with radium packs at a distance of two to three centimetres (this was done before our association with the department). A "series" of treatments consisted of the total amount of

radiation given within a period of about two months. The administration of more than two erythema doses to the skin over one area in a series was considered a large dose; one or two erythema doses as a moderate; and less than one erythema dose as a small dose. It was found that those cases which improved did so with small or moderate amount of irradiation. In twenty-one cases in which clinical improvement occurred following the treatment with X-ray and radium, the dosage was small in seven, moderate in thirteen, and large only in one case.

Radiotherapy of pathological fractures could be evaluated in seven cases. Four fractures did not unite. Three of these had very little and one a large amount of irradiation. A fracture of the middle third of the humerus showed marked callus formation after two small X-ray treatments. Bone sclerosis, but no union, followed the administration of moderate amounts of X-ray treatment to a fracture of the surgical neck of the femur. Complete bony union of a fracture of the left clavicle was noted following very small radiation doses from a 3-centimetre radium pack. Union of pathological fractures in several cases of cancer of the breast has been observed without any treatment (Harold Neuhof, personal communication).

A remarkable case not included in this series should be mentioned in this connection. It is a case of generalized skeletal metastases from a carcinoma of the breast with involvement of the skull, the spine, the pelvis, *etc.* The various skeletal metastases were irradiated with small doses of X-rays and improvement followed. The skull was not exposed to X-rays, yet comparison röntgenographs showed marked diminution in the size and number of the osteoclastic metastases in the skull. Evidently something more than local X-ray effect took place in this case.

*Metastases to the Central Nervous System.*—It was mentioned in the beginning of this paper that clinical differentiation of compression, extension, and metastases in the central nervous system from cancer of the breast is difficult if not impossible. Since only nine of the twenty-five cases suspected of brain metastases and four of the thirteen cases diagnosed as spinal-cord metastases were examined post-mortem, our figures as to frequency of occurrence of metastases into the central nervous system are not quite accurate. As a matter of fact, it may be questioned whether true metastases occurred in the spinal cord or whether all cases with cord symptoms were either compression by, or extension from a metastatic focus in the corresponding vertebræ. Symptoms of metastases to the central nervous system occurred in nearly 21 per cent. of the 168 cases investigated. Sixty-eight per cent. of the cases (seventeen of eighty-one) with neurologic evidence of brain involvement also showed positive röntgenographs of skull metastases. *Vice versa*, 68 per cent. of the patients with röntgenographic evidences of metastases to the skull also showed definite symptoms of brain invasion.

The symptoms of the onset of the brain invasion varied. They can be divided into three groups:

- A. Cases showing signs of gradually increasing intracranial pressure (three cases).
- B. Cases with signs of increasing intracranial pressure and localizing neurologic signs of cerebral, cerebellar or brain stem involvement (eleven cases).
- C. Cases showing neurologic signs of cerebral, cerebellar and brain stem invasion without increased intracranial pressure (ten cases).

In 68 per cent. (seventeen of twenty-five) of the brain metastases and in 70 per cent. (nine of thirteen) of spinal-cord cases, the involvement occurred during the terminal stage of the disease. The survival period after the appearance of neurologic evidence of involvement in the eight pre-terminal brain cases varied from seven to twenty months, and in the four cord cases from five to thirty-one months. The effect of radiotherapy could be evaluated in five pre-terminal brain cases and in three pre-terminal cord cases. Three of the brain cases had shown early signs of increasing intracranial pressure. In one case, as a result of moderate X-ray therapy, headache disappeared for a period of four months, then re-appeared and was again relieved for a short time, then the patient succumbed to brain stem involvement. In another, headache was relieved for six months then recurred as a terminal feature. At autopsy extensive involvement of the dura without invasion of the brain was found. In the third case headache, vomiting, and convulsions of the right upper extremity disappeared following a small radium application and little X-ray treatment to the opposite side of the brain. The survival period in these three cases after the onset of clinical evidence of brain metastases were eleven, eighteen, and twenty months respectively. It is noteworthy that the generalized skeletal metastases in these patients also responded well to the X-ray therapy which they received. Of the two cases which gave neurologic signs of localized involvement of the brain, one improved following a small radium pack, while no improvement was noted in the other, after apparently well-placed, moderate X-ray therapy. Several other cases are not quoted in detail as they occurred in the terminal stage. They showed temporary regressions of headache, and diplopia, and disappearance of facial palsy for periods varying from a few weeks to three months. Of the three cord cases, two showed definite relief of pain from moderate X-ray dosage. No beneficial effect was seen in the third case.

#### SUMMARY

One hundred and sixty-eight cases of metastases to various body systems from carcinoma of the breast were studied from the time of discovery of the tumor to the time of death. Forty-eight per cent. had skeletal metastases, 15 per cent. showed brain metastases, and 8.7 per cent. spinal cord-involvement.

Of the eighty-five cases of metastases to the skeleton and central nervous system thirty-two were examined post-mortem, sixty-seven were corroborated histologically, and sixty were graded according to the histological evidence of

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malignancy into three groups: Grade I or least malignant, Grade II or moderately malignant, Grade III or most malignant.

It was found that three time factors varied in direct relation with this grading: *a*, the time interval between the discovery of the tumor and the onset of symptoms of skeletal metastases; *b*, the survival period after discovery of the tumor; and *c*, after symptoms of skeletal metastases. These three periods were markedly shortened with increasing malignancy; thus the average interval between the discovery of the tumor and the onset of metastases was 46.5 months for Grade I, 29.1 months for Grade II, and 10 months for Grade III. The survival period after the discovery of the tumor for cases in Grade I was 50.2 months, Grade II 23.5 months, and Grade III 17.3 months. The survival period of pre-terminal cases after the onset of skeletal metastases was 19.7 months for cases in Grade I, 16.2 months for those of Grade II, and 10 months for those of Grade III. The survival of cases with marked glandular differentiation was somewhat longer than those which did not show this characteristic.

The term of the patient's life following the discovery of the tumor was divided into two periods, a terminal period, that is the last third or in cases lasting more than three years, the last year of life, and pre-terminal or earlier period; 55 per cent. of the skeletal metastases occurred in the pre-terminal period.

Age apparently had no influence upon the survival period and most cases occurred between the ages of forty and fifty.

The primary tumor arose in the right breast in forty-three and the left breast in thirty-eight cases.

Of forty-five cases occurring in the pre-terminal stage, the skeleton was the primary localization in 82 per cent. However in only 16 per cent. did it remain limited to the skeletal system. In the rest it was associated with metastases to other parts of the body.

The most frequent localization in the skeleton of the pre-terminal cases was the lumbo-sacral spine, the femur, pelvis, dorsal spine, skull, ribs, scapula, and humerus, in the order mentioned.

Pain was the first sign to call attention to skeletal metastases in 75 per cent. of the cases. The time interval between the first complaint of pain and the appearance of definite röntgenologic evidence of skeletal metastases was followed carefully in nine cases. It was found to vary from a few weeks to one year.

Pathologic fractures occurred as a terminal manifestation of the disease and were encountered in 26 per cent. of the cases. Of seven treated pathologic fractures only one united after a radium application.

X-ray and radium therapy were very useful agents in control of pain. They caused diminution and at times marked temporary regression of the clinical and röntgenographic signs of skeletal metastases. Clinical improvement started twenty-four or forty-eight hours after the first treatment and



lasted from a few weeks to three years. Moderate dosage seemed to be sufficient and sclerosis of the radiated bone was observed in several cases.

Clinical signs suggesting metastases to the central nervous system occurred in 21 per cent. of the one hundred and sixty-eight cases investigated and were usually a terminal manifestation. Clinical differentiation between compression, extension and true metastases into the central nervous system was impossible. Sixty-eight per cent. of the cases diagnosed as brain involvement showed positive röntgenograms of skull metastases and all cases diagnosed as spinal-cord metastases showed röntgenographic evidence of a preceding metastasis to the lumbar vertebra at the same level. In a few cases temporary regression of signs of increased intracranial pressure and localized brain involvement occurred following moderate dosage of radiotherapy.

#### CONCLUSIONS

The prognosis of skeletal metastases from cancer of the breast varies with the histological character of the primary tumor or its metastases. This influences the survival period after the discovery of the tumor and after the onset of the metastases, and has a bearing upon the time interval between the discovery of the tumor and the onset of skeletal metastases.

Pain usually precedes positive röntgenographs of skeletal metastases and is the most important symptom of skeletal invasion.

Clinical signs suggesting metastases to the central nervous system from cancer of the breast occurred in about one-fifth of the cases investigated. In more than half of the brain cases there were associated metastases in the skull and in all of the spinal cord cases there were metastases in the corresponding vertebrae.

Radiotherapy relieves pain in a great number of cases of skeletal metastases. In a few cases of skeletal metastases it produced a remarkable temporary regression and in a few cases of invasion of the central nervous system it also caused palliation.

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## PAPILLOMA OF THE DUODENUM

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TUMORS of the duodenum are of such relatively infrequent occurrence as to justify the placing on record of cases as they occur, although the literature of the subject is beginning to assume considerable proportions. Perhaps the most exhaustive articles to date are those of Golden, in the *American Journal of Roentgenology and Radium Therapy*, and Eliason, Pendergrass, and Wright, in the same publication. Anyone interested in the literature on the subject should consult these comprehensive résumés.

Almost every type of benign tumor encountered elsewhere in the intestinal tract may be found in the duodenum. Instances of adenoma, calcified submucosal fibroma, adenoma of Brunner's glands, myoma, polypoid thickenings, hæmangio-endothelioma, lymphangio-endothelioma, *etc.*, are recorded in the literature.

It is worthy of note that in a considerable number of cases, tumors of the duodenum were associated with pathological conditions elsewhere in the intestinal tract—multiple polyposis, carcinoma, cholelithiasis, *etc.* Tumors of the duodenum seem to be confined to no particular age; reported cases range from infants of a few days to individuals of over seventy years. There seems to be no particular pathognomonic picture associated with their presence. They give rise, as a rule, to symptoms that suggest more strongly, perhaps, than anything else, duodenal or gastric ulcer or carcinoma. Hæmorrhage, either macroscopic or microscopic, sometimes very severe, is common. Pyloric obstruction, more or less pronounced, is often present. The usual diagnosis is a provisional one of duodenal ulcer. In general, though, there seems to be less actual pain than one is accustomed to associate with true ulcer. In a few cases, the diagnosis has been made by Röntgen-ray examination, usually with the aid of the fluoroscope. It is based upon the demonstration of a characteristic filling defect in the shadow of the barium-filled duodenal bulb. In our case, the diagnosis was definitely made by Dr. Thomas R. Brown, with the aid of the fluoroscope, which diagnosis was later confirmed by plates taken by Dr. Charles A. Waters, whose plates, together with his interpretation of them, are appended.

In differentiating these cases, Golden attaches considerable importance to the presence or absence of a six-hour gastric retention. He states that "in the presence of a filling defect in the duodenal bulb, suggesting non-malignant tumor, a six-hour gastric retention may be considered as evidence in favor of a growth arising in the stomach and prolapsing into the duodenum, and the absence of such a retention as indicative of a growth arising in the duodenum itself." In our case there was no retention, the stomach emptying

within normal limits. In addition to their comparative rarity, the especial interest in these cases attaches to the matter of diagnosis and treatment, especially in view of the ever-present tendency of papillomatous growths of the mucosa to degenerate into carcinoma.

The chief reason for reporting this case is to emphasize the fact that this is one other condition that must be borne in mind in making a diagnosis in the case of gastric or duodenal trouble. It emphasizes, too, the necessity for a very careful fluoroscopic study of all such cases. While it may not be possible in every case to make the diagnosis, certainly the fact that a correct diagnosis has been made in a certain percentage of the cases reported shows that the attempt should be made.

Where the growth has a small, well-defined pedicle, ligation and excision of the entire thickness of the mucosa are probably all that is necessary. One, however, should never forget the possibility of malignant degeneration. The specimen in our case showed that it had already begun, although not recognized until examination of the microscopical slides showed its presence, so that nothing short of resection would have offered a cure.

The outcome in our case was extremely unfortunate. It represents another of those calamities of surgery of which Paget wrote so eloquently many years ago and which, in spite of every precaution, happen now and then to every operating surgeon of experience.

REPORT OF CASE.—(Dr. Thomas R. Brown.) Patient, male, aged sixty-eight years, was admitted to the Union Memorial Hospital November 23, 1929, on account of pain in the epigastrium when stomach was empty. His illness was of six months' duration. Previous to that time, had no digestive trouble. Bowels regular. Trouble began as epigastric discomfort, most pronounced during the forenoon; not much in evidence in the afternoon or at night. Sometimes pain was relieved by an alkali or something to eat; no nausea or vomiting; no gross blood in the stools; no jaundice.

For the past two months symptoms had been aggravated, with very little intermission. With reduction of the amount of food ingested, patient felt more comfortable. This was followed by moderate loss of weight.

His past history presented nothing of interest.

Examination revealed a well-nourished man. Mucous membranes rather pale; pupils somewhat irregular; react normally to light; tongue slightly coated; teeth negative. No palpable glandular enlargement. Heart and lungs negative. Blood-pressure 150/96. Abdomen showed liver with upper limit normal; edge palpable two fingers' breadth below costal margin; spastic sigmoid slightly tender. Nothing else made out by palpation. Rectal examination negative.

The test meal showed an achlorhydria—free acid 0; total 8. Urine was negative. The one specimen of stool examined showed occult blood present; no parasites. The hæmoglobin was 92 per cent.; the white blood cells, 9,400. Blood Wassermann was negative.

The fluoroscopic studies of the gastro-intestinal tract showed a stomach normal in tone and function, fish-hook in type, absolutely normal in contour. The duodenal cap was extremely interesting; irregular, not filled in the centre, but filled as a shell around the periphery. This same picture was seen in repeated examinations. The duodenum was moderately dilated but could never be filled in any position in which the patient was put.

From the history, which was somewhat suggestive of duodenal ulcer, from the achlorhydria and from the fluoroscopic studies, the diagnosis was made of a papillomatous growth of the duodenum, and operation was advised.

According to the X-ray report made by Dr. Charles A. Waters "the pylorus seems to be all right, but, as the barium goes through the duodenum, it spreads out in a fan-shaped manner, as though it were encircling a mass. The marginal contours of the duodenal cap seem to be perfectly normal. A series of films showed a definitely enlarged duodenal cap with a smooth contour, but with a very multilocular type filling defect, which seems to be inside the cap.

*Impression.*—There is no doubt that there is a lesion present, but the etiological factors are certainly very confusing from an X-ray point of view. It would seem almost certain that a neoplasm should be considered. In any other part of the intestinal tract, this type of filling defect would warrant a diagnosis of papilloma or polyposis.



FIG. 1.—Film of the stomach and duodenum immediately after the ingestion of the barium meal showing the smooth contour of the duodenal cap with its multilocular, vacuolated appearance within the duodenum and the depression of the pyloric sphincter by the papilloma acting as a ball valve.

*Comment.*—In studying Fig. 1, one can see at a glance that the filling defect in the duodenum is a very unusual one, and that a diagnosis such as papilloma from this film is not such a hazardous guess. However, in neither the fluoroscopic examination by Doctor Brown and myself nor in a considerable number of films was this visualized with any such clearness as shown in Fig. 1. This fact is mentioned in order to show the necessity of making films of fine detail in gastro-intestinal examinations, in addition to the fluoroscopic examinations."

*OPERATION.*—(Dr. J. M. T. Finney). November 25, 1929. Gas-ether anæsthesia; high right rectus incision. Examination of the stomach and duodenum revealed a soft mass about the size of an olive in the lumen of the first part of the duodenum. The anterior duodenal wall was incised over this mass, exposing a lobulated papillomatous tumor with a rather broad base. It was felt that if the tumor were excised, considerable

## PAPILLOMA OF THE DUODENUM

narrowing of the lumen of the duodenum would inevitably result. Resection was, therefore, decided upon.

The typical operation was performed, removing terminal 2 inches of stomach, pylorus and upper  $1\frac{1}{2}$  inches of duodenum, followed by a Polya anastomosis. No difficulty of any kind was encountered.

The patient stood the operation well, but the evening temperature showed considerable elevation. The temperature continued to rise, in spite of anything that could be done. The pulse became accelerated with the rise of temperature, finally reaching, on the third day, temperature  $104^{\circ}$ , pulse 140. There was evidence of a generalized peritonitis, and, on the fourth day, the patient died with every evidence of septic infection.

*Autopsy.*—Upon reopening the abdominal incision, a rather large pocket of pus was found in the abdominal wall, not communicating with the peritoneal cavity. The peritonæum showed mild, early, generalized peritonitis. About 300 cubic centimetres of slightly blood-tinged fluid in the abdominal cavity. There were two or three definite, small, localized abscesses present, one about the upper margin of the anastomosis—the largest contained 200 cubic centimetres of thick, creamy pus, apparently arising about the stump of the duodenum. The suture line of the anastomosis was everywhere tight, except at the upper angle, where there was a questionable leak. Stump of duodenum seemed tight. Cultures showed streptococcus and bacillus coli.

*Diagnosis.*—Acute generalized peritonitis with localized abscesses.

*Comment.*—This was one of four cases, all operated upon within a few days, with the same technic, assistants and material, all of which cases showed a similar post-operative picture. Three of the four cases died. There had been no infections in the operating room previously; there were none subsequently. All operating was at once stopped, and an exhaustive study of the entire operating technic, staff, materials, *etc.*, was made by Dr. W. W. Ford, of the Bacteriological Department of the Johns Hopkins University, all of which proved negative in every way, except for a particular brand of catgut, which had been used in these cases, and which showed repeated cultures of an anaërobic diptheroid.

This experience, which was most unfortunate, shows how important it is to make frequent tests of everything that comes into contact with an operative case. The firm making this particular catgut was at once notified of the findings. There has been no trouble since.



FIG 2—Photograph of the specimen after removal

*PATHOLOGICAL REPORT.*—(Dr. W. G. MacCallum) "The specimen consists of the pylorus of the stomach and the first part of the duodenum, which contains a polypoid

Wm P. Didusch 1929

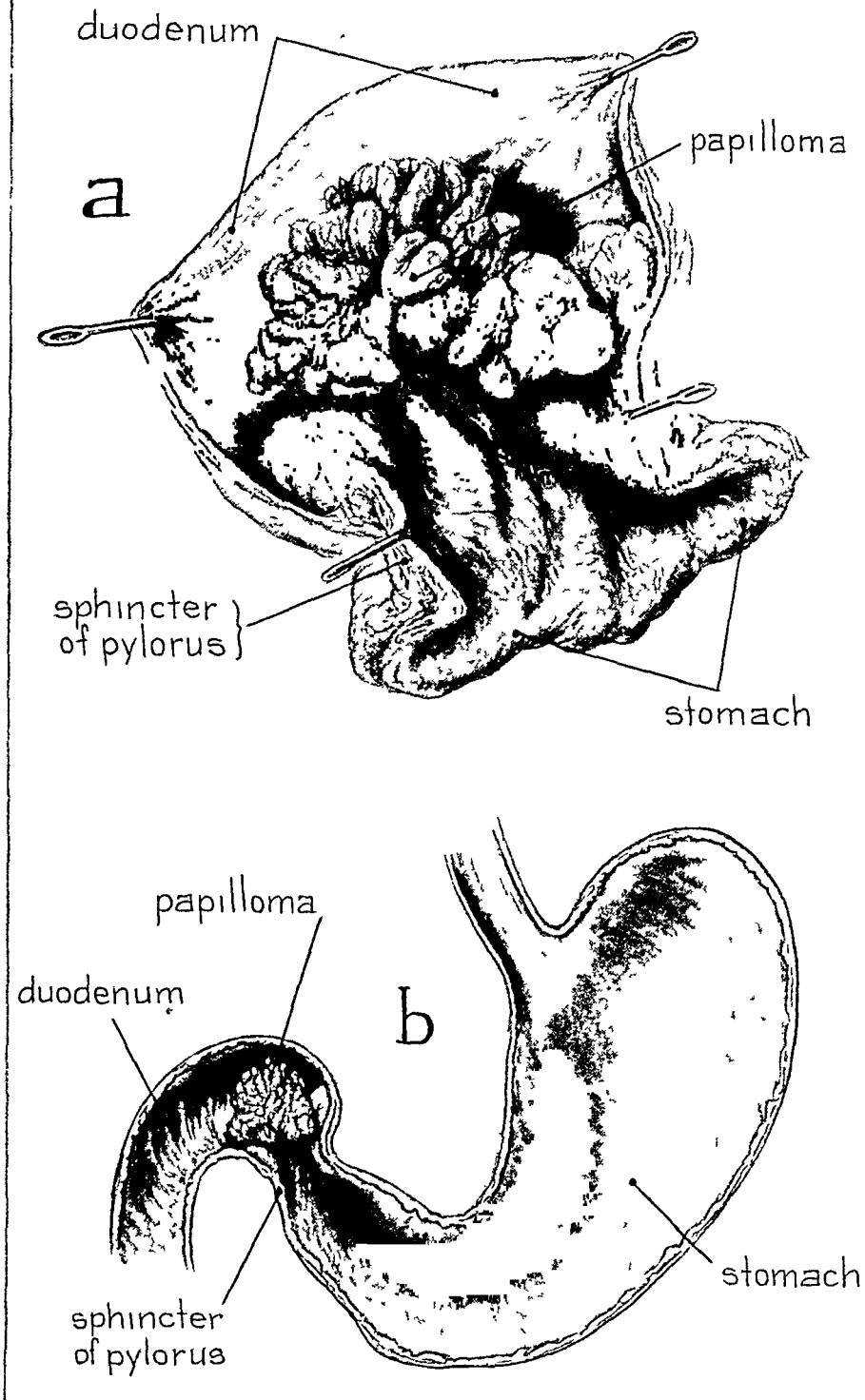


FIG 3—*a*—Shows the arrangement of the papilloma in the duodenum  
*b*—Diagrammatic sketch showing the relative size and location of the papilloma with reference to the pyloro duodenal junction

## PAPILLOMA OF THE DUODENUM

growth extending into the lumen. There is a fold of tissue where the pylorus is usually seen, and below this point there is duodenum. However, at another point in the circum-

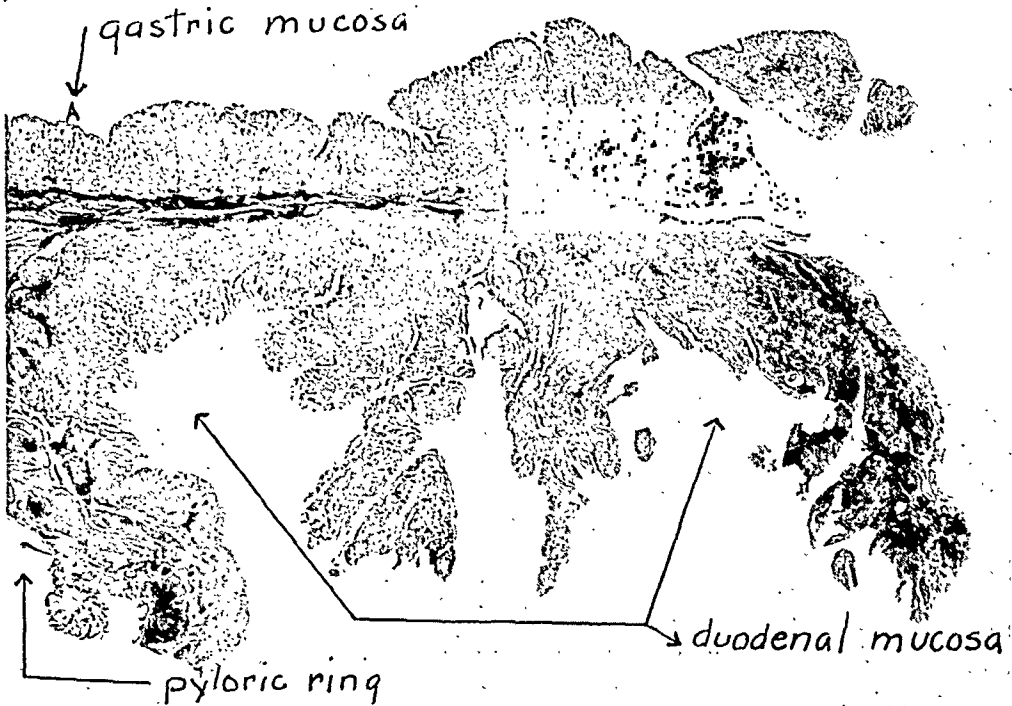


FIG. 4.—Microphotograph showing the papilloma and the extraordinary formation of the polypoid epithelium.

ference, at the same level, the mucosa of the stomach is seen to extend downward and up on to the polyp, so that it would appear that the polyp is really derived from the

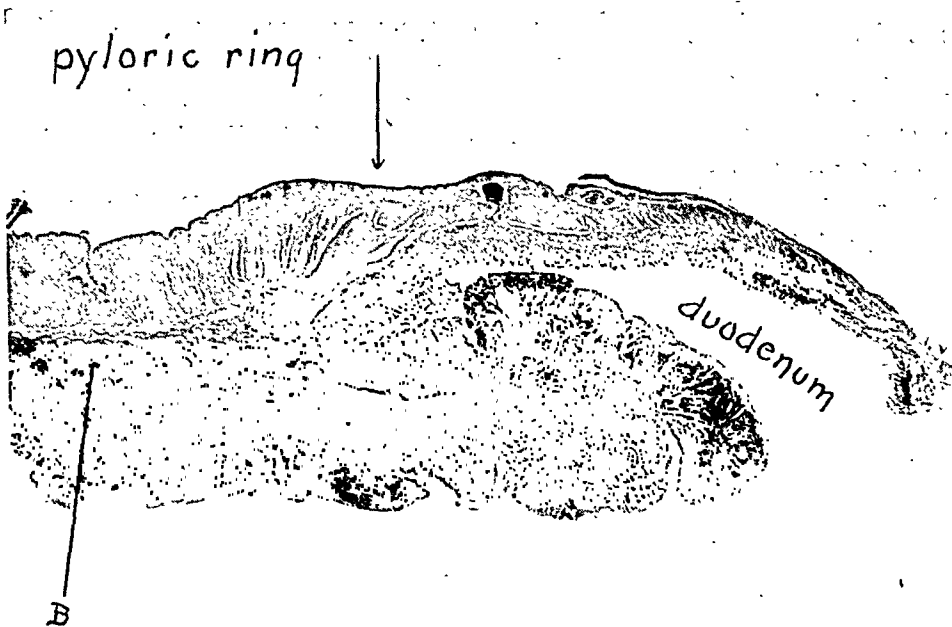


FIG. 5.—Microphotograph showing the pyloric sphincter and duodenum with invasion of the deeper layers of submucosa of the stomach.

stomach and has been dragged down to lie in the lumen of the first part of the duodenum. This may, however, not be borne out histologically.

"The polyp itself forms a mass measuring 4.5 centimetres from base to tip, and 5 centimetres in diameter in its outer portion. There are, however, other masses of the



same tissue which grow out from the base of the polyp in a more sessile manner and completely encircle the lumen just below the pylorus.

"On longitudinal section through the more pedunculated portion, the stomach mucosa is seen to extend down over the polyp, measuring 1-2 millimetres in thickness. Club-shaped processes project from the pedicle in all directions."

Fig. 2 shows the gross specimen after removal.

Fig. 3 shows a drawing, illustrating the arrangement of the papilloma in the duodenum and its relationship to the pylorus.

*Microscopic Description.*—"The sections taken longitudinally through this hanging, polypoid mass show gastric mucosa on one side, and duodenal mucosa on the other. Fig. 4 is a microphotograph of the longitudinal section through the pylorus and duodenum. The gastric mucosa at 'A' clearly shows an extraordinary formation of ramifying, glandular downgrowths in patches, scattered in the more normal mucosa. In the polyp, the epithelial structures become very disorderly, remaining gland-like, but very irregular in form. There are tubular glands in the stroma, which are drawn up into the polyp, but one cannot be sure that they are not due to tangential cuts of a space between two folds.

"In Fig. 5, the same structure is found, except that in this section the polyp is more sessile. At the point marked 'B' there are very definite downgrowths of epithelium into the submucosa of the stomach. They look like tubules of epithelium lying in lymph channels, and there is a small lymphoid mass in which epithelial cells are lodged. Here they are in minute subdivision and distributed in small groups in the lymph-node and in the form of very small tubules. I think this is a definite indication of a tendency to malignant invasion. No tumor has been found deeper than the submucosa, but there the invasion of lymphatics is extensive."

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# CARCINOMA PERIGASTRODUODENALE

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TUMORS of the external coats of the stomach are not frequent and all are of the type of connective tissue sometimes mixed with epithelial proliferations. Among them sarcomata are most common and for the purposes of this paper only sarcomata and other tumors arising from external layers of the stomach and having an exogastric development will be considered later. Epithelial tumors growing exogastric are unknown to me.

Here is presented a case of epithelial tumor arising probably from the subserous stomach-duodenum coat and which for convenience I shall call carcinoma perigastroduodenale.

CASE HISTORY.—B. A., forty-three years of age. Nothing important in his family and in his personal history. In May, 1915, after a raid of Austrian destroyers against his native town on the sea and especially after an air bombing, he began to feel agitated, sleeping irregularly while he was compelled to work hard to change his home. In the beginning of August severe toothache prompted him to have a medical examination. He had already observed that his abdomen had grown rather hard on the right side, what he believed to be a faecal accumulation notwithstanding all his functions were regular. The doctor told him that it was a tumor and other doctors said the same afterwards. X-ray examination confirmed the diagnosis. I saw him November 10, 1915. He was rather thin and pale. Subjective symptoms were absent, except for some eructations after meals, and a sensation of drawing down from under the sternum when he was standing. Appetite, stomach and bowel functions normal. Physical examination of chest negative.

The abdomen showed a slight prominence on the right side of the mesogastrium reaching the median line mesially and almost the anterior axillary laterally. Palpation showed a mass of about 9 by 8 centimetres of irregular surface, hard, with an inferior lobulated margin, better limited than the superior one where from time to time one could perceive a soft swelling vanishing under the pressure of the hand. The mesial border was the less definite and while one could almost grasp the tumor externally and inferiorly and in part also above, it was impossible to do so on the medial side. The tumor was slightly movable with respiration and could be pushed freely from right to left and the contrary, but much less from up downwards or in the opposite direction. The most prominent part was dull on percussion; above and laterally the resonance was tympanitic. No pain during the examination.

X-ray report states: The stomach is pushed to the left, the great curvature has the shape of a sack and reaches a point three to four fingers under the transversal umbilical line. The shadow of the tumor corresponds to the pyloric portion of the stomach, which after 8½ hours is not completely emptied; there are no contractions. Movements imparted to the tumor are transmitted to the stomach. No mention is made about pylorus and duodenum conformation. The colon was regularly filled and without abnormalities. The diagnosis appeared evident—a tumor belonging to the stomach, but outside of it. It was uncertain whether it had grown directly from its outer coats, or, originating from some other structure outside of it, had developed toward the stomach and become attached to it. About its nature also nothing definite could be said as no sign was present which suggested the many existing possibilities. Certainly it was not

a cancer of stomach proper for the radiologist had not seen any sign of it; nor did the patient have symptoms pointing to such a tumor.

Formerly a case of an uncommon tumor of the stomach had been operated upon by me. It was a large tumor located in the middle of the greater curvature and extending down between the layers of the gastroduodenal ligament and adhering to the transverse colon. The mucous coat of the stomach was ulcerated and for that reason the tumor was catalogued as stomach cancer with extrinsic development. It proved later, on reviewing the sections, that this was not so. But this case caused me to think that the one in discussion could be similar to that and consequently the diagnosis of cancer of stomach with extrinsic development was thought to be the most probable one.

*Operation.*—Ether narcosis. Longitudinal transrectal incision on the right. It was easy to lift the tumor out of the wound and to see that it was larger than it had appeared (Fig. 1). It belonged to the pyloroduodenal part of the stomach, of which the walls appeared normal. The pylorus and duodenum were pushed upwards and the latter also outwards, very considerably enlarged and stretched also in the length. The



FIG. 1.—Perigastroduodenal carcinoma.



FIG. 2.—Sagittal section through duodenum and tumor.

lower pole of the tumor was adherent to the right portion of the transverse colon. The tumor was partially enclosed posteriorly in the gastroduodenal ligament as if, originating from the stomach walls, it had pushed down and behind the layers of that ligament, being free from it in front.

The great omentum was ligated in portions under the growth, and after it had been made clear that the transverse colon was not involved, the tumor was separated from this; then a part of the great and small omentum was detached from the two curvatures, the stomach clamped and cut well above the antrum, was turned to the right and the duodenum made free for a few centimetres under the tumor and cut. The tumor was removed as Fig. 1 shows and the duodenum, stretched as it was, showed such a large stump that it could be united end to end to the stomach. As far as the inspection could ascertain, nothing abnormal was observed in the upper right abdomen. Recovery was uneventful.

The patient returned in April in a cachectic condition, showing a large liver metastasis, and died from it toward the end of April.

*Anatomical Study of the Tumor.*—Fig. 1—represents it almost in its natural size. It is a solid, rather hard mass, 10 by 8 by 7 centimetres. The surface and the contour

is lobed, the color reddish, with brown hæmorrhagic spots and stripes. It is attached largely and firmly to the great curvature in proximity of the pylorus, and to the first portion of the duodenum which is greatly enlarged. The gastrocolic ligament lies partly behind the tumor, and the great omentum hangs down from its lateral and lower edge, so that a portion of the posterior surface is covered, while the anterior is free.



FIG. 3.—Frontal section of tumor. In (A), a thin normal pancreas layer.

Examination of the mucous coat of stomach and duodenum showed it to be movable or independent of the growth, and normal.

A sagittal section through duodenum and growth (Fig. 2), near the pylorus where the attachment seems closer, shows that the tumor has a thin capsule except above where it is fused with the duodenal wall whose layers are independent but for the serosa. Same result gave another section cardinal warts of the pylorus. The section



FIG. 4.—Parenchyma of the tumor.



FIG. 5.—Tubular formations on the left. In the middle an oral formation similar to an island. Note the abundance and structure of the connective tissue.

surface is yellowish gray with many small soft areas and spaces and with a large central cavity containing necrotic hæmorrhagic masses.

A frontal section of the tumor cut as in Fig. 3 shows better the relations of it with the duodenal walls. We see all the coats independent of the growth but in one part the outer muscular coat is involved, also the serous coat for a larger extension.

Here no capsule can be traced, also none farther posteriorly, where a thin layer of normal pancreas removed with the duodenum is almost fused with the growth. Microscopically the separation from the pancreas is evident.

The capsule is made of very fine connective fibres, with thin, flat, elongated nuclei, disappearing in the most central layers; it is infiltrated above by the growth in the form of thin, oblong strands, apparently in vascular spaces. The tumor is almost uniformly necrotic, and it is possible to follow in it for a great distance a connective

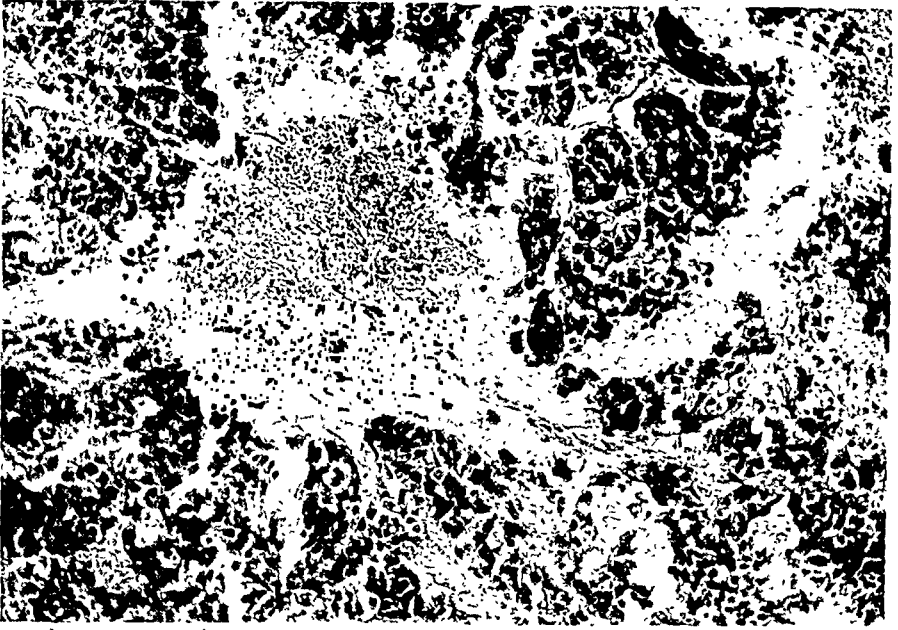


FIG. 6.—In the centre, a necrotic mass. All around lobule-like formations.

framework which, starting from the capsule, divides the tumor mass into large areas, and these again into smaller irregular ones.

The parenchyma of the tumor (Fig. 4), is arranged in oblong masses, which are divided by the connective framework into smaller portions, that is, into strands and



FIG. 7.—The cell structure of the tumor.



FIG. 8.—To show the extensive and various cellular degenerations.

columns of cells. These are resting peripherally on the fibres of the framework, while in their central parts appear hæmorrhagic and necrotic spots. Generally the solid columnar structure is the prevailing one, but in some parts cavities or lumina of different sizes are demonstrable, surrounded by one or more layers of cells, so that in these points the structure has an adenomatous appearance (Fig. 5). Here the connective

stroma is abundant and largely cellular. In other parts the structure is more lobular (Fig. 6).

The cells of the tumor are of different forms and sizes. As the growth is mostly necrotic and the unfavorable vascular conditions are extensive, even in the best preserved parts there are degenerative changes of the cells of various character. This makes it difficult to describe a cellular type of the tumor. Mostly in the best preserved parts the cells are cubic, roundish in shape, with an oblong, rather big, nucleus, more or less deeply stained (Fig. 7). The protoplasm of the cell is not well limited in contour and the cells seem to merge into other cells. In other parts the shape is more polygonal and flat, and where there are lumina or cavities surrounded by cells these are distinctly cubic or almost cylindrical, forming a complete layer all around, limiting



FIG. 9 —Extensive necrosis—a small vessel, and, around it, cellular masses are preserved.

the cavities very regularly, as is proper for glandular ducts or lumina and with nuclei generally toward the base of the cells.

In Fig. 5, near the adenomatous part, is a small mass of cells forming an almost oval and limited body. The cells in this are smaller. Degenerative and various changes of the cells are almost the rule.

Fig. 7 shows the protoplasm of most cells, as clear, divided in portions by thin threads; in many appear vacuoles which may take almost all the cell, pushing the flattened nucleus to the periphery. Hydropic degeneration, steatose, cellular inclusions, and gigantic cells of difficult interpretation appear also here and there (Fig. 8). Through destruction of cells, spaces are originated which are clearly distinguished from the adenomatous spaces, as the former have not a regular shape and the surrounding cells are also irregular in form and disposition.

Mitoses are not numerous and not regular.

Vessels are scanty and of only a capillary size; vascular spaces are more numerous, and the cells mostly in contact with it. This perivascular disposition is best visible in

the periphery of necrotic zones where everything is dead but for some few vessels and vascular spaces surrounded by cellular masses, giving the appearance of a perithelial disposition (Fig. 9). The cells here are smaller, rather round and their protoplasm not well limited, with round nuclei less deeply stained.

The stroma of the tumor deserves a brief description. We said that there is a capsule and thin septa starting from it and dividing the growth. This stroma can be called trabecular and it is the main frame. Besides there is the delicate network dividing the columnar strands; this is made of very fine fibrils penetrating even between small groups of cells, and having elongated, very thin nuclei. This can be called fibrillar.

But as shown in Fig. 5 there are large areas of tissue with fusiform cells, and in some sections such areas are surrounded by the fibrillar framework as if it were another kind of tissue having its own properties and growth.

Summarizing the previous descriptions we may say that attached to the stomach and duodenum was found a large solid tumor mostly encapsulated, composed of polymorphic, not well differentiated elements disposed in columns and strands, infiltrating the subserosa of the duodenum and the capsule, with scanty adenomatous portions, and alveoli of smaller cells and tubes, with a poor thin vascular arrangement; hence extensive massive necrosis and cellular degeneration, with a polymorphic connective stroma, resembling a parenchymal embryonic tissue partly differentiated, in a way to be compared to an unstriped muscular tissue.

Both parenchyma and stroma are, then, of embryonic character without a typical differentiation, but having a disposition which may allow us to speak of its probable origin.

The general lobular arrangement of the growth, its cells with tendency to grow cubic, though irregular and polymorphic, the appearance of adenomatous portions and of solid small tubes, speak for a typical growth of glandular epithelium, where the solid form prevails over the adenomatous proper.

A comparison with the thin layer of pancreas removed with the tumor and in close contact with it, shows a similarity of general disposition, and also few degenerative changes in its epithelium comparable to that of the tumor.

The seat of origin of the tumor could be supposed to be in the subserous coat of stomach or duodenum, or outside of these and penetrating later into them. Certainly the mucous and muscular coats and the pancreas could not be its origin. In any case it is necessary to think of an embryonic germ either in the stomach or duodenal walls or near them as the source of the growth.

The simplest supposition is that it is derived from an aberrant pancreas. We know their frequency and their possible location all along the gastro-intestinal tract and chiefly near the pylorus and the duodenum, according to Delhougne in the proportion of 58.3 per cent., and in the subserosa in the proportion of 15 per cent. They are miniature complete organs, well differentiated and generally without special structural particulars which dispose

them to grow into a tumor. But besides these can be found incomplete formations, that is, ducts alone without glandular tissue, but with Langerhans' islands, islands alone (Lauche), or ducts and glandular tissue with masses of epithelial cells not completely differentiated, or with embryonal character.

That these aberrant pancreases may be the origin of tumors is admitted and for the adenomyoma of the stomach, especially, seems to be proved. But these are clinically unimportant, and the literature does not show cases of true neoplasm with progressive development whose origin can be traced in aberrant pancreas elements. Mathias, Beutler and Herxheimer do admit this as a possibility, but their cases are the least probable. These were extremely small tumors made of pancreatic germs with proliferation of adenomatous or myomatous character having then organoid structure, without any sign of progressive growth and certainly not to be considered true blastomata.

The cases of Askanazy, too, do not speak for the possibility of such origin as none of them is a true progressive tumor, and he himself says that the aberrant pancreas has not yet been found in relation with a true neoplasm. The same opinion has been expressed by Delhougne.

Such affirmations, though very important, cannot have an absolute value in refuting that possibility, and before doing so I think it is necessary to compare my case with cancers of pancreas proper. These are supposed to originate from the lining cells of the ducts, from the mucous glands of the ducts, from tubuli or gland tissue proper and from Langerhans' islands.

The duct-cell cancers are admitted to be cylindrocellular chiefly and of the adenomatous, cubic or polygonal, less differentiated, and the general structure of a solid tumor. Those derived from mucous glands of the ducts are characteristic of mucus production and the cells though irregular in size and shape have a tendency to be cylindrical (Helly-Rheiner). Such a schematic division can be accepted as an orientation.

Tumors in the pancreas, as elsewhere, do originate from elements which have the capability of regeneration, and to these cells is inborn the property of differentiation in various stages. Besides the same tumor cells, according as the tissue where they grow and the conditions of their development, may change considerably in shape and disposition. For these reasons we may find in the same pancreas cancer, solid and glandular formations, and cells of various shapes, even a tendency to polymorphism, with variations in the staining properties, and with various types of degenerations.

Comparing my case with true pancreas cancers, we find that in my case there is a general disposition of a solid lobular tumor with round, polygonal, cubic elements and with tendency to polymorphism. Rare are adenomatous formations, and very extensive the degenerations. This can be admitted as being close to a pancreatic solid tumor of glandular origin. But there are differences which are, chiefly, a more embryonic, undifferentiated character of the cells in general, their perivascular disposition in many parts and the



presence of large areas of connective tissue which is not a tissue reaction but, as I shall discuss later, a part of the tumor itself. For these reasons and for the theoretical ones above quoted, I believe that my case can be compared in some part to a glandular pancreas tissue cancer, in some others not, so that it is not proved beyond refutation that it can be of aberrant pancreas gland origin.

Can we think of it as coming from isolated aberrant Langerhans' islands? These are known to be present in the stomach and intestine very seldom without accompanying pancreatic tissue, but with ducts.

Following Lauche only four cases can be considered as positive, that is a case of Saltykow in which islands and ducts were found in the mesentery, a case of Delhougne, one of Askanazy in the stomach, and his own which he calls carcinoid of the small intestine. M. B. Schmidt also described a case in which many small carcinoids of the small intestine were found, with a combination of islands, pancreatic tissue and carcinoid areas. Saltykow derives the intestinal carcinoid from islands tissue, and calls them "tumores pancreatici intestini." In none of these cases were found characteristic qualities of a beginning true blastoma.

Here, too, before making a conclusion, it will be convenient to examine the neoformations known to arise from islands in the pancreas itself.

But before examining these cases I believe it is proper to review what is known about the so-called independence of the islands, and their capability of regeneration and proliferation. The absolute independence and delimitation of the islands from the surrounding glandular tissue is variously admitted. It seems to be possible, but usually there is a relation between the one and the other (Otani). There is the same difference of opinion about the possibility of the islands to transform into glandular tissue and the opposite. Laguesse, the chief exponent of this doctrine, and his pupils call it a "balancement," while Weichselbaum and many others deny it completely. They believe that in adult life neoformation of islands happens as in the foetal life, that is, from pancreatic ducts, and in course of time becomes exhausted. The regeneration can be from elements of the islands but especially from the ducts. The finding of islands tissue in connection with the glandular tissue is not a proof of a reciprocal transformation but it represents the final fixed developmental condition in which one can recognize the origin of islands from the glandular tissue and from the ducts. This view of Neubert is accepted also by Kraus.

The islands, then, constitute a highly differentiated tissue with determined functions and cannot be considered as a tissue in continuous germination.

According to Walz there are cells, which could be called *basal cells*, not only in the ducts but scattered between the glandular elements of the tissue and the islands. From these could be formed islands and glandular tissue, and eventually these cells could proliferate abnormally and remain in a stage of lower differentiation, forming a tumor which could be called "*basaliome*."

From these facts we are brought to admit as extremely difficult to accept

the possibility of tumors arising from cells of the islands already differentiated. Tumors having origin from them have been described *adenomata* and *carcinomata*.

The first bears then the name of "*insular adenomata*" to separate them from the glandular tissue adenomata. Such a name should be applied only to veritable tumors, and not to proliferations of islands tissue which are a high grade of compensative hypertrophy (struma or adenoma insularis) in diseased pancreas, or perhaps developmental abnormalities in a normal pancreas.

Twenty cases are in the literature from the first case of Nicholls to the last of Warren. All were extremely small, well-isolated growths characterized by a resemblance of their elements to those of the islands. None had any sign of active proliferation or malignancy and clinically they have no importance. The one described by Walz as "basaliome" is to be compared to that of Rollet and according to Gruber is to be considered as a solid adenoma of insular formation.

These cases have been described as *malignant adenoma* originating from islands in the pancreas.

A case of Soprana's.—It was a cystadenoma proliferating as a cancer invading the organ extensively and with metastases and peritoneal implantations. The structure was chiefly of a tumor originating from glandular and duct elements, but there were well-limited formations similar to islands tissue and he thinks that this too contributed to the growth together with ducts and glandular cells. There are no proofs for such an opinion and probably these limited formations must be considered as a reactive proliferation.

A case of A. Vecchi's.—Man, aged sixty-three years, had had a big tumor in the left hypochondrium for nine months. At operation the large mass, which was retroperitoneal, was enucleated. Autopsy showed that it had developed laterally to the pancreas whose tail reached the bed of the tumor and was complete. Tumor of 18 by 20 centimetres; weight 2.5 kilograms; lobed, hard, encapsulated, at section rose-whitish with spongelike portions containing mucous substance. Microscopically masses and strands of cylindrical, prismatic, high, conic cells, with definite contours disposed regularly along the fine vessels; rich nuclei, oval, rich in chromatin. Many degenerations of the cells, hence the spongelike parts, and hyaline degenerations in the stroma. Posteriorly, inside the capsule, was found a small island of pancreatic tissue with islands and ducts. The growth was invading some of the islands intimately, mixing its elements with those of the islands in such a way as to make one think that their origin was in these. Other islands showed alterations to be interpreted as a proliferative reaction. He calls this growth an adenoma and thinks that it had arisen from the islands of a supernumerary caudal pancreas lobe of which a residual portion was still present. The reasons were the intimacy and affinity between islands and tumor cells, the similarity of these with islands cells, and their perivascular disposition.

I could not find in the figures given by Vecchi such cellular similarity; and the proof of cellular affinity and intimacy has no worth. The islands seem to be passive, infiltrated. The presence of a small pancreatic lobule almost intact is a proof against, as, if the growth had arisen in this, it would have completely destroyed it when attaining such a size.

Cancers of the pancreas originating from islands have been described by Fabozzi. In five cases he found in the zones between the tumor and the pancreas, an increase in number and size of islands, with hyperplasia and fusion forming large, cellular masses connected with the tumor and having the same staining and histological qualities.

Subsequent investigators have denied not only this origin of pancreas cancers in general, but also the possibility of a cancerous proliferation from the islands, and Fabozzi's theory seemed forgotten when later Horgan found cellular proliferations in cases of hypertrophy of the islands pointing to a possible malignancy, but without a real tumor, and two cases were published in America which deserve a special mention; the first published by Russell, Allan, Power and Robertson, the second by Thalhimer and Murphy.

These have in common a severe hypoglycæmia expressing itself in the first, a man of forty years with attacks of faintness and weakness occurring more frequently in course of time for eighteen months, and resulting in coma if food or sugar intake was delayed; and in the second, a woman of fifty-seven years, with attacks characterized by somnolence followed by great restlessness and irritability lasting one day followed by one day of almost continuous sleep. These attacks grew more frequent, until at last they were occurring every day with convulsions without loss of consciousness and followed by coma. The details of these cases and the complete investigations made in the first are extremely interesting, but not regarding our present question. The man was operated upon at the Mayo Clinic and a hard, nodular pancreas and tumors in the liver were found. A short time afterward he died and an infiltrating tumor of 5 centimetres was found in the tail of the pancreas with yellowish nodules and a small cyst and metastases in the liver. Microscopically the pancreatic tissue was seen to be replaced extensively by tumor cells embedded in a dense connective stroma and arranged in irregular strands and islands. The cells were of irregular size and shape, and staining reaction and arrangement, strikingly resembling cells of Langerhans' islands. The cytoplasm was well stained with slight basophile reaction, and the cell masses arranged about capillaries usually in two rows, occasionally in alveolar form, but with no evidence of glandular structure. Many degenerations were found in some parts, but no mitosis except in the liver tumors. Because of these characteristics and others, which anyone interested in the case will see better in the original paper, the authors conclude that the tumor is a carcinoma, arising primarily in the islands cells, and that there is evidence of hyperinsulinism from this tumor and especially from its liver metastases.

The second patient died in coma during one of the attacks. Nothing was found at the necropsy but about at the junction of the body of the pancreas with the tail a tumor nodule appeared, of 1.5 by 1 centimetre, slightly prominent, ovoid, firm, creamy white, well demarcated, incompletely encapsulated and seeming to invade the pancreatic tissue, but without metastases. Microscopically there was a parenchyma composed of cells which appeared to be identical with the cells of the islands, divided in masses and strands irregularly by dense connective tissue, and in some places there were small groups of tumor cells so isolated by connective tissue as to appear identical with normal islands, no typical mitoses. In other places were few cells larger than normal island cells of irregular shape, with hyperchromatic nuclei, atypical, and as if they were about to undergo proliferation. In some places and toward the edge of the tumor were aspects of malignancy characterized by slow growth and invasion. The author's conclusion is that the tumor was a carcinoma of a low grade of malignancy, originating in the islands cells and giving clinical manifestations of hyperinsulinism. This interpretation was accepted by Robertson, Wilder and Bensley.

The preceding review shows:

First.—That tumors arising from isolated aberrant Langerhans' islands have been an extreme rarity and none possessing the qualities of a progressive growth.

Second.—That malignant adenoma from island of an aberrant pancreas does not exist except for Vecchi's case which is not beyond refutation.

Third.—That it is possible, though extremely seldom, to find a true cancer in the pancreas with the characteristics of Langerhans' islands structure.

This last possibility has been proven now by two cases. But is it equally proven that these two tumors had their origin in the islands? If we think of the peculiar structure of the islands and of their characteristics, to be a well differentiated specifically functioning tissue with scanty proliferative regenerative power, it seems more justifiable to admit that tumors composed of cells of the Langerhans type are produced by proliferation of embryonic elements having the same properties as the ones which primarily originated the islands. Without thinking of an embryonal anlage separated from its parent and included in the pancreas we can admit that normally the cells which have the power of regenerating the islands are the formal cause of a tumor, for such elements are undifferentiated, have a high reproductive power and from them can come blastomatous formations which may repeat atypically either one of the pancreas components or some together. One ascribes this property to the cells described by Walz as above reported, or to those contained in the so-called indifference zone of Schapers and Cohen—that is to cellular proliferating centres having embryonic properties from which regeneration should come and later possibly tumors.

It would be far simpler to have a unitarian conception of the formal genesis of pancreatic tumors, and this conception could be formulated: The elements which have the function of regenerating the different tissues of the pancreas preserve in the adult life, some of their embryonic qualities and may, for unknown reasons, proliferate atypically and according to the various stages of differentiation these atypical cells reach, we see tumors of different composition. It is natural to see more frequently tumors of glandular and duct structure than tumors of islands structure, these being the highest in differentiation.

This conception does away with the useless or preconceived tentatives to assign to a definite tissue or elements of an organ the primitive source of a growth, which is almost always impossible. The fact that a growth repeats atypically some structure does not mean that its origin was in the ripe elements of the same.

Coming now from this digression to my case I find that the comparison of it with Langerhans' islands in diseased conditions and with the published tumors, can give some arguments in favor of a similarity.

These are: The distribution of the cellular masses sometimes in strands; the close connection of the cells as in the islands; the contact with the capillaries in many instances, without a separating *membrana propria*; the small

size of cells in many parts; the uncertain limitation of their protoplasm; the slight basophile staining (as far as could be ascertained). Besides, it is possible to find here and there a small areole (Fig. 5) rather well limited, with small cells resembling an island.

Against this origin from islands, or against the insular structure of the tumor, is the prevailing embryonic character of the cell masses, with no decisive differentiation, the few glandular formations and the quality of the special stroma, not dense, fibrous, as observed previously, but delicate, rich in cells, giving the impression of a tissue having a constituent part in the growth.

My conclusion is that such origin cannot be proved.

The third possibility is the origin from an embryonal germ included in the subserosa of the stomach or duodenum.

That such inclusions are really existing and perhaps more frequent than it is known, is shown by the publications of Askanazy illustrating various qualities of such inclusions, and trying to put them in relation with the cancer of stomach. In some of them pancreas lobules, stomach mucosa invaginations, ducts and cysts were mixed together, and in one also epithelial lobules without lumina resembling L. J. The connective stroma of such findings is also various and I think the fact is especially noteworthy that in some it was a soft tissue with abundant stellate formed cells or a delicate fibrillar tissue with flat nuclei.

Those formations are called blastoid by the author who discusses the possibility of cancer arising from them and later invading the mucous coat and ulcerating it so that in an advanced stage it is impossible to recognize its true origin. Whatever it may be for the cancer of stomach, it is important to remember the presence of such inclusions and the possibility of their transformation in blastomata.

As such formations are to be explained only by admitting the inclusions of entodermic germs it is evident that the future evolution may be in various directions: In one case the tendency may prevail to a complex of tissue, a blastoid or organoid formation, or to mucous membrane formation; in another to a pancreas tissue or to a less typical tissue nondifferentiated.

In my case, the conditions of the epithelial growth are these: Generally a solid mass, rarely of glandular type, with a type of cell more embryonic and difficult to compare with cells of a typical organ, but so disposed as to imitate a lobular structure; here and there perivascular disposition, and small areolæ of smaller cells. The stroma of the tumor can be so distinguished as there is: A capsule with its septa running through the tumor, having a fibrous and lamellar structure, and connective-tissue areas with triangular or starlike irregular cells in loose formation; moreover strands of fusiform cells regularly disposed in fascicles and such that a distinction between fusiform connective cells and small unstriped muscular fibres is difficult. These connective formations cannot be interpreted as a reaction of tissue to the invading tumor, first, because of their cellular structure and then of their

disposition in masses and bundles; secondly, because the tumor has no development into other tissue or organs from which a connective proliferation could arise. They are then a constituent part of the tumor.

These considerations bring me to conclude that this tumor is a peculiar one, solid, with scanty adenomatous formation, with a peculiar connective tissue, with cellular types and disposition to be compared to pancreatic atypical glandular structure, to islands atypical structure, but not so well definite to assign to one or to the other, or to both together, being generally too much atypical and undifferentiated. Forcibly we are induced to think of a more primitive and undifferentiated germ as its formal cause, that is an entodermal one which in its later blastomatous development took the direction of an atypical pancreas structure but so atypical that none of the types has been reproduced in a characteristic way.

*Location of the Tumor.*—Two possibilities I have considered already. *First*—The origin from embryonic elements in the subserosa. *Second*—From such ones in the gastrocolic ligament.

The first seems the more probable. Like many exogastric connective-tissue tumors, this grew where it was easier, that is, downwards, occupying in part and displacing the gastrocolic ligament, and infiltrating only later the longitudinal coat of the duodenum. If it had been born inside the ligament, this would have covered its anterior surface completely, which, instead, was free from it.

Embryonal formations included in this part of the omentum are unknown to me. For analogy with Saltykow's case, of pancreas germ in the mesentery, made of ducts and islands, and with the possible presence of entodermic elements in lymph-nodes (as in a lymph-node of pancreas pancreatic tissue was found by Nakamura) the presence of embryonal germs could be supposed possible.

*Clinical Considerations.*—The diagnosis of rare cases is generally not and cannot be made correct, and diagnostic refinements suggested in some instances after operations or necropsies, are mostly a consequence of theoretical or so-called logical considerations very seldom adaptable to practice. I shall not venture to say that cases like mine will be correctly diagnosed in the future, but their possibility will be considered.

Direct diagnoses of a perigastric duodenal tumor could be deduced by such signs: The presence of a movable tumor which could be demonstrated to have a relation with the stomach and duodenum without alterations of their walls as proper of carcinoma. This can be reached partly by air insufflation, and better by accurate X-ray investigation. In my case the rays showed the stomach pushed to the left and the greater curvature having the shape of a sac and situated much below the umbilical line, while the tumor shadow was continuous with the pyloric portion. The stomach had a notable delay in emptying. That seems to me enough to make a diagnosis of tumor in relation with the stomach.

A differential diagnosis should consider the seat of origin of the tumor and its nature. The possibilities are these:

*Carcinoma of Stomach.*—This may, in two instances, appear as a large tumor extrinsic to the organ. The first is, when having origin from the mucous coat it grows outside the walls, forming a large mass apparently attached only to the organ. I know only a case of Konjetzny and one of Knoflach and Eichelster from Eiselsberg's Clinic, which was developed toward the diaphragm. I myself have seen one such case, and another which was thought to be similar proved later to be probably a malignant carcinoid of extragastric origin.

The second instance is when a small stomach growth gives origin to large glandular metastases which impose for an extrinsic gastric tumor, as perhaps everybody has seen from time to time, in the lymph-nodes of the small curvature, but very rarely in those subpyloric or subfundal, or in the omentum forming in this a large mass. In a case of Konjetzny there was in the pyloric region a tumor of about 5 mk. size, and the metastasis in the omentum was larger than a foetal head.

*Carcinoma of Transverse Colon* with extracolic development, that is, in the gastrocolic ligament, or with metastases in the lymph-nodes.

This was seen by me in one case, and recently V. Ascoli has published such a case diagnosed by him and operated by R. Alessandri successfully.

According to my experience, extrinsic development of colon cancers is rather more frequent than in those of the stomach and not always accompanied by typical symptoms.

*Sarcomata and Other Benign Tumors of the Stomach and rare cases, like dermoids* (see two cases reported by Eusterman and Senty from Mayo's Clinic) may develop outside when they have a large base in the organ walls, growing in different directions. The most common is downward as they originate chiefly in the anterior or posterior wall near the greater curvature, and their development can proceed between the layers of the gastrocolic ligament. (Pseudonetz tumors of Borrmann.)

Subjective signs, like pain and impaired function, may bring one to locate the growth correctly, but such symptoms either were missing, or vague and not typical, and in such cases various diagnoses have been made as one can see in reviewing the literature of stomach sarcomata. We may expect that insufflation of the stomach and especially an X-ray investigation will throw more light.

Reviewing the experience made in cases of sarcomata and extrinsic growths of this organ we find that in none of those submitted to X-rays was the diagnosis made. A negative X-ray finding will not be sufficient to preclude the origin of a tumor from the stomach. I believe that such negative cases will be rarer and rarer in the future if doubtful cases will be examined repeatedly, and if peculiar deformation and displacement of its position will be

found, the diagnosis can be directed toward the suspicion of extrinsic gastric tumor. Pneumoperitonæum and gastric insufflation may be practiced and aid toward a correct diagnosis (C. Desseker).

*Tumors of the Omentum.*—When solid and non-infiltrating, a condition which is very rare, these tumors may draw the stomach downwards and give origin to mistakes in diagnosis. I have not found decisive symptoms for a differential diagnosis. But the X-ray examination can certainly distinguish the relation of tumor and stomach.

The possibility of tumors developing in the upper part of the abdomen are many; and it is not the scope of this paper to consider all or to analyze the possible errors with tumors of other organs. These have been described by Alessandri, Lofaro, Konjetzny, Amelung and others, and I refer the reader to their papers.

In conclusion, there are some rare epithelial tumors arising from the walls of stomach or duodenum, which deserve a special pathological and clinical consideration. These tumors, together with connective-tissue tumors of stomach, especially sarcomata, and with stomach and colon cancers growing exogastric, constitute a class of abdominal tumors which in the future must be included in the diagnostic possibilities, and sometimes may be diagnosed correctly if the clinical and anatomical facts will be kept in mind.

In cases like my own the name of perienteric carcinomata would be more correct perhaps; a name which, being more general, eliminates suppositions about origin, which cannot be proven adequately.

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THE PREVENTION OF CARCINOMA OF THE GALL-BLADDER

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IN RECENT years, much attention has been directed towards the prevention of cancer by the education of the public concerning those various lesions which are generally considered to be precancerous. These efforts have, however, been concerned chiefly with cancer of the lip and mouth, the stomach, the breast, the rectum and the female genital organs. It is an astonishing fact that little or no emphasis has been placed upon the possibility of the prevention of cancer of the gall-bladder. In a paper presented by Doctor Ewing<sup>1</sup> himself, at the International Symposium on Cancer at Lake Mohonk, New York, in 1926, on "The Prevention of Cancer," nothing whatever was said about the possibility of the prevention of cancer of the gall-bladder. Moreover, I have not been able to find any article that has been published, at least in recent years, dealing particularly with the prevention, although, in occasional writings, attention has been directed to the frequency of carcinoma in this region.

It is difficult to understand why cancer of the gall-bladder has been neglected in all of the educational work that has been done by the American Society for the Control of Cancer and other similar organizations. It would seem that there could be only two reasons for this neglect: first, that it is considered to be a rare disease, and, second, that there would seem to be no way of preventing it. It is the purpose of the present paper to attempt to show that both of these ideas are erroneous.

The great frequency of carcinoma of the gall-bladder as compared with

| Name of authors  | Buday     |           | Bejach    |           | Redlich   |           | Feilchenfeld |           | Riechelmann |           | von Berencsy and von Wolff |           |
|--|-----------|-----------|-----------|-----------|-----------|-----------|--------------|-----------|-------------|-----------|----------------------------|-----------|
| The number of autopsies from which the statistics have been compiled | 5,530     |           | 6,808     |           | 5,002     |           | 5,022        |           | .....       |           | 19,908                     |           |
| Number of cases of cancer .....                                      | 336       |           | 692       |           | 496       |           | 507          |           | .....       |           | 2,314                      |           |
| The organ  | Male      | Female    | Male      | Female    | Male      | Female    | Male         | Female    | Male        | Female    | Male                       | Female    |
|  | Per cent. | Per cent. | Per cent. | Per cent. | Per cent. | Per cent. | Per cent.    | Per cent. | Per cent.   | Per cent. | Per cent.                  | Per cent. |
| Esophagus.....   | 6.21      | .....     | 20.3      | 0.8       | 17.3      | 2.8       | 21.3         | 1.6       | 20.0        | 1.4       | 11.88                      | 0.61      |
| Stomach.....   | 38.42     | 16.36     | 36.5      | 31.3      | 39.9      | 39.6      | 39.9         | 25.2      | 46.6        | 34.1      | 48.90                      | 20.45     |
| Intestine.....   | 5.64      | 1.05      | 8.2       | 6.1       | 4.2       | 6.1       | 4.3          | 4.3       | 3.7         | 3.9       | 5.34                       | 2.75      |
| Gall-bladder.....  | 1.12      | 2.10      | 1.9       | 8.5       | 3.5       | 10.8      | 1.2          | 9.1       | 3.9         | 9.5       | 2.77                       | 10.18     |
| Breast.....  | 0.56      | 5.80      | .....     | 12.5      | 0.35      | 12.2      | .....        | 12.6      | 0.3         | 8.3       | 0.09                       | 6.85      |
| Ovary.....   | .....     | 14.78     | .....     | 2.1       | .....     | 5.1       | .....        | 4.7       | .....       | 4.0       | .....                      | 8.16      |
| Uterus and vagina  | .....     | 45.40     | .....     | 13.3      | .....     | 14.1      | .....        | 17.7      | .....       | 24.6      | .....                      | 35.99     |
| Uterus.....  | .....     | 44.35     | .....     | .....     | .....     | .....     | .....        | .....     | .....       | .....     | .....                      | 34.85     |
| Vagina.....  | .....     | 1.05      | .....     | .....     | .....     | .....     | .....        | .....     | .....       | .....     | .....                      | 1.14      |

carcinoma of other organs is shown in the table compiled by von Berencsy and von Wolff:<sup>2</sup>

It will be seen from an examination of this table that carcinoma of the gall-bladder has a very marked tendency to occur more often in women than in men and that it constitutes in most of the statistics between 8 and 10 per cent. of all carcinomas in women. It would seem fair, therefore, to conclude from the various statistics which have been already presented that carcinoma



FIG. 1.—A typical example of carcinoma of the gall-bladder associated with calculi.

of the gall-bladder is a comparatively frequent disease and because of that reason deserves our attention.

In this country, also, the frequency of carcinoma of the gall-bladder seems to be about as great as in the table given above. The mortality statistics<sup>3</sup> of the Bureau of the Census for 1926 state that in the registration area of continental United States there were, in 1925, 9,558 deaths from cancer of the liver and gall-bladder. In 1926, there were 9,635 deaths. It is true, of course, that all of these deaths were not due to primary carcinoma

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of the gall-bladder, but since other carcinomas which cause metastases to the liver are listed separately under the œsophagus, stomach, intestine and rectum, the presumption is strong that most of these cases listed as carcinoma of the liver and gall-bladder were either primary carcinomas of the gall-bladder or primary carcinomas of the liver. The latter tumor is known to be rare. It would seem fair, therefore, to conclude that the majority of cases listed as carcinoma of the liver and gall-bladder were primary carcinomas of the gall-bladder. Primary carcinoma of the other portions of the bile tract is known to be rare as compared with carcinoma of the gall-bladder. During the same two years, the total deaths from cancer of all kinds were as follows: in 1925, 95,504 deaths, and, in 1926, 99,833 deaths. This would indicate that carcinoma of the gall-bladder constitutes roughly between 8 and 10 per cent. of all carcinomas and that its incidence for the general population is about 9 per 100,000. This is a very considerable number of deaths from this cause. As listed in the mortality statistics, deaths from cancer of the gall-bladder are about three times as frequent as from that of the lip, about one and one-half times as frequent as all cancers of the lip and buccal cavity, about twice as frequent as cancer of the rectum, of about the same frequency as cancer of the breast, about two-thirds as frequent as cancer of the female genital organs, and a little less than one-half as frequent as carcinoma of the stomach. It should not necessarily be inferred from these figures, however, that the occurrence of carcinoma of the gall-bladder in comparison with other organs is actually so high as it would seem to be, because nowadays many people with cancer of the other parts of the body mentioned are cured by surgical and other methods and, therefore, many cases of those cancers would not appear in the mortality statistics. The figures which are given merely show the deaths from the various types of cancer.

Concerning methods of prevention, the most outstanding fact is that carcinoma of the gall-bladder, in the great majority of cases, is associated with gall-stones. The frequency of the relationship between carcinoma of the gall-bladder and gall-stones is so great that various statistical studies have shown that in from 69 (Musser<sup>4</sup>) to 100 per cent. (Janowski<sup>5</sup>) of cases of carcinoma of the gall-bladder, biliary calculi are present. Lentze,<sup>6</sup> who has recently studied the statistical incidence of gall-stones in cases of carcinoma of the gall-bladder from an extensive review of the literature, considers that cholelithiasis is practically always the primary condition. In this opinion he is not alone. Almost all of those who have studied this question believe that the evidence is overwhelming that when calculi are present they have preceded the development of the carcinoma. They should, therefore, be considered as being a definitely precancerous lesion. It seems unnecessary to present here in a detailed manner all the evidence in favor of this view. It is, perhaps, sufficient to call attention to a few facts. The opinion which has been expressed by some writers that the calculi are the result of the carcinoma seems to be supported by no evidence. For example, Siegert<sup>7</sup> showed that, although calculi were present in ninety-four cases of a total of

ninety-nine primary carcinomas of the gall-bladder which he collected, they were present in only two of thirteen cases of metastatic involvement of the gall-bladder. Rolleston and McNee<sup>8</sup> collected twenty-five other cases of metastatic involvement of the gall-bladder and found calculi present in only one. Therefore, in the total of thirty-eight cases of metastatic carcinoma of the gall-bladder, gall-stones were present in only three cases, an incidence of 8 per cent., which is well within the normal limits of incidence of gall-stones. What would seem to be conclusive evidence of the importance of the factor of cholelithiasis in the production of carcinoma of the gall-bladder seems to have been supplied by the experiments of Leitch,<sup>9</sup> of the London Cancer Hospital Research Institute, who found that when he introduced human gall-stones and even ordinary pebbles into the gall-bladders of guinea-pigs there resulted a remarkable change in the epithelium of many of the cases, which he considered to be entirely characteristic of carcinoma. Although metastases of distant organs did not occur, nevertheless, there was marked invasive growth of the carcinoma into the liver, the omentum and even into the chest wall. The illustrations accompanying Leitch's article are very convincing. It would seem, therefore, that there can be no reasonable doubt that the presence of calculi in the gall-bladder predisposes the individual to a carcinoma of that organ. This would seem to be particularly the case if the patient is a woman beyond the age of forty. It is unnecessary in this article to discuss how the gall-stones may operate to produce the carcinoma.

Another important consideration is the question: In what proportion of cases of cholelithiasis does carcinoma of the gall-bladder occur? The various statistics which have been published on this point vary greatly. Lentze<sup>6</sup> found, in a collective study, that in 557 cases of cholelithiasis in women over thirty-nine years of age, there was an associated cancer of the gall-bladder in 5.1 per cent. Rolleston\* states that 4.5 per cent. of all cases of cholelithiasis are accompanied by carcinoma of the gall-bladder. Moynihan\* gives 5 per cent., Riedel\* 7 to 8 per cent., Mayo-Robson\* 10 per cent., Schröder 14 per cent. In our own cases at the Barnes Hospital 8.5 per cent. of all cases of stones in the gall-bladder have been associated with carcinoma of that organ. According to Leitch, the lowest incidence reported is that of Candler, who found in post-mortem statistics from an insane asylum an incidence of only two cases of carcinoma in 315 cases of calculi. The highest incidence, according to Leitch, is that reported by Slade, who found 30 per cent. It is, of course, probable that the incidence reported by surgeons, and coming from the general hospitals, is somewhat higher than that of the general population, because practically all of the cases of carcinoma of the gall-bladder sooner or later reach the hospitals, but many of the cases of ordinary cholelithiasis without carcinoma do not. It would seem reasonable to conclude, however, that at least 4 or 5 per cent. of women in the cancer age, who have gall-stones, will develop carcinoma of the gall-bladder and

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\* Quoted from Leitch.

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perhaps further study will show that the incidence may actually be much higher.

If we accept the idea that gall-stones represent a definite precancerous lesion of the gall-bladder, the most obvious consideration in the prevention of this condition is the question of the possibility of diagnosing biliary calculi. The improvement in diagnosis of lesions of the biliary tract, which has been made possible by cholecystography, now enables us to diagnose biliary calculi with practically 100 per cent. of accuracy. It is true that the stones themselves cannot always be visualized, but in our experience at the Barnes Hospital every case of biliary calculi, without exception, which has come to operation, has revealed itself on cholecystographic examination, either by actual visualization of the calculi or by the demonstration of an unquestionably pathological gall-bladder. It would seem, therefore, that no particular difficulty should be encountered in the recognition of this very definite precancerous lesion.

A most important consideration is, of course, the question as to whether or not we should advise the operative removal of a calculous gall-bladder, or at least of its contained stones, from the point of view of cancer prevention entirely apart from the other more usual operative indications. This question naturally involves the consideration of the risk of cancer on the one hand as compared with the risk of operation on the other. The operative mortality in uncomplicated cases of cholelithiasis before there has been much damage to the liver, to the heart, to the kidneys, *etc.*, should not be more than 1 per cent. This is, approximately, one-fourth or one-fifth of the danger of death from carcinoma. At the hands of experienced surgeons, the operative mortality, even including all of the bad risks which present themselves as examples of long-neglected biliary-tract disease with many incurable complications, is still about only 3 per cent. or less. Our own mortality at the Barnes Hospital during the last three years has been 1.5 per cent. This series has included patients of all ages and with practically all of the known complications of biliary-tract disease. Deaths from all causes which have occurred in the hospital have been included in the operative mortality. It is significant, however, that most of the deaths have been due to incurable complications of neglected disease of the biliary tract. Younger patients, in better physical condition and with fewer complications, would almost certainly present a much lower operative mortality. From the standpoint of cancer prevention, it would seem to be our duty to inform patients with gall-stones that, in general, they have a greater chance of dying from carcinoma of the gall-bladder than they would have by a properly performed operation. This phase of the question is in addition to any other features of the case which should be regarded as ordinary indications for operation. The danger of cancer is especially great in women past forty, and this danger is probably increased if they come from cancer families with an inherited predisposition to its development.

## SUMMARY

Since gall-stones seem to have an etiological relationship to the development of carcinoma of the gall-bladder in nearly all cases, the occurrence of most if not all cases of carcinoma of the gall-bladder could be prevented by cholecystectomy in cases which present evidence of gall-stones, regardless of the presence of those symptoms which would ordinarily compel a patient to have an operation. The diagnosis of gall-stones is now easily and accurately made by cholecystography. In uncomplicated cases of gall-stones there is less risk of death from the operation of cholecystectomy than from the development of a carcinoma of the gall-bladder, particularly if the patient is a woman of middle age. Contrary to the general opinion carcinoma of the gall-bladder is not a rare disease, but a very common one. It constitutes approximately 8 or 10 per cent. of all carcinomas.

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## ELECTROSURGERY IN GYNÆCOLOGY

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MEN who fill our professional ranks, whether in medicine, religion, or law, are habitually conservative. This salutary mental attitude expresses itself peculiarly in our communal relations; namely, when a new idea appears which is more or less subversive to old notions and practices, he who originates the idea must strike sledge-hammer blows in order to secure even a momentary attention. This must then be followed by a long, patient propaganda of proclamation and advertising until in the grand finale the public, indifferent at first, is aroused, proceeds to discuss, and finally accepts the iconoclastic proposal as a long-accepted fact of its own invention and asks wonderingly, "Why such a pothor? What after all is there new about the thing? We knew it all long ago!"

Such is the history of the therapeutics of radium about which the public is just opening and rubbing its eyes after a quarter of a century of sleep. And so, too, has it gone with the electrosurgery marvelously wrought out by William Clark, of Philadelphia, in 1908-1910, and promulgated with all the documentary evidences and data necessary to establish its rights of eminent domain over a new and large arena in the surgical realm.

In this latter field, however, we are still in the proclamation stage when success waits upon iteration and reiteration—both beneficent procedures, for which no apology is necessary—while we continue to hammer at the general surgeons' doors and shout aloud our incontestable attainments, as we beg for a meed of generous recognition in all our large hospitals.

Here we supplant our ancient procedures in the operating amphitheatre with electric current oscillations of a million or more a second and regulable from a minute needle-point spark up to a flashing, withering, sword-like flame, made superficial or penetrating at will. With George A. Wyeth's knife (acusector) we cut tissues as a hot knife goes through butter, or we dry the structures to a powder, or, again, we boil or coagulate without carbonizing, the current exerting its potency at or close around a needle point or a small ball, the active agent held in the operator's hand remaining a cold field.

Unlike radium, which is a ray therapy, electrosurgery is thoroughly surgical and at once a vigorous, insistent competitor with those age-long badges of our profession—scalpel, ligature, needle and suture, supplanting these time-honored instruments in their own arena and in appropriate cases relegating them to the *Rumpelkammer* as mediæval, crude, antiquated. Although the field of this new electrosurgery is a broad one, its preferential work lies conspicuously in the destruction of cancer where in numerous instances it reaches



a perfection of *ne plus ultra*. I adhere as my theme in this brief memorandum to one of its more limited fields where it does not appear altogether at its best advantage. I speak of cancer in the female generative tract. One who wishes to judge it for the first time should observe a skilled operator in the surgery of the mouth or of the brain.

In gynæcology, electrosurgery is preferable in:

1.—Cancer of the external genitals: vulva, clitoris, Bartholin's glands and the external urethral orifice.

2.—The destruction of metastatic or suspected inguinal glands.

3.—Cancer of the vagina in its primary form and the destruction of metastatic nodules in the vaginal wall.

4.—Cancer of the cervix, cooking and destroying the tissues until the cervix can be reamed out in a hollow cone for the better lodgment of an effective radium treatment.

5.—Lower abdominal surgery, cooking superficial cancerous nodules remaining after the enucleation of the large parent mass, whether uterus or ovaries.

6.—A scirrhus nodule in the wall of the intestine, which can be necrotized even through the entire thickness of the wall and then left *in situ* after drawing the peritoneum over the area with fine silk sutures.

7.—Papillomatous tufts on the peritoneum, which can be withered down to the base and out of existence by an exposure of a fraction of a second duration, requiring no ligatures or sutures. In this way many can be wiped out in a minute, a precious saving of time.

8.—Areas of carcinoma left on or in the pelvic wall after an extirpation.

9.—Enlarged glands on the pelvic floor, which are punctured and coagulated thoroughly and left *in situ*, as well as any gland at a bifurcation of a large vessel, saving a prolonged, difficult operation at a critical period after a panhysterectomy.

10.—Papilloma of the bladder, forming a brilliant and speedy way of attack either by cooking its pedicle if it is pendulous, or by coagulating the flat, raspberry masses, stopping hæmorrhage and extirpating the tumor or reducing the mass for radiation.

The value of electrosurgery in all these situations lies in the perfect control of the current which can be applied as effectively at any reachable distant point by a stiff wire as on the surface of the body; that is to say, at the vaginal vault, deep in the pelvis, in the bladder through the aëroscope, up in the rectum at the pelvic brim in the knee-chest posture, or down in the larynx or in the fauces, and even in the trachea and bronchi.

The advantage over scalpel and suture is perhaps more apparent in that the tissue cooked and sterilized *in situ* is often not removed but advantageously left to be thrown off spontaneously in a few days. In treating large glands, it may be well at times to puncture and coagulate thoroughly and then to incise and curette away all the friable tissues, to be followed by a thorough cauterization of the capsule from within. A metastatic gland

lodged in the bifurcation of a large vessel is admirably managed in this way by an experienced operator.

The value of electrosurgery in vulvar cancer is at once apparent in carcinoma of the entire vulva, always an awkward knife, forceps, and ligature operation. Here the cutting current reduces the bleeding of the incision to a negligible minimum. Then follows a careful dissection, undermining while raising the mass. Any larger vessel seen as it is approached through the fat is caught with delicate forceps slightly curved at the tip and divided; finally, the few vessels so controlled are sealed by touching each forceps with the coagulating current when they wither and are sealed (Grant Ward). So *pari passu* the new operation advances to its finale in far less time than with a scalpel dissection. Great care should be taken not to contaminate the wound during such a knife-and-fork operation. The flashing current can be used advantageously to sterilize any ulcerated areas on the surface.

It must not be reckoned a small matter here that there is a great saving of ligatures as well as of time in operating, not to pass unnoted the few and simple instruments sterilized. Nor, again, should we overlook the fact that the post-operative discomforts are greatly lessened, while these cases are either ambulant at once or in a very short time, substantially increasing the turnover of the hospital. There is also, I think, a wise inclination on the part of experienced electrosurgeons to leave many of these sterile wounds open and to treat them with a 2 to 3 per cent. mercurochrome solution daily, protecting them under simple dressings from exposure and contamination. Granulations spring up with surprising rapidity, and a soft flexible scar is the outcome—a matter of extreme importance in many familiar situations, mentioning the periphery of the eye as an example. The field of local anæsthesias is extended to the satisfaction of many patients.

While we sing the praise of this new electrosurgical field, he will do best by his patient who also thoroughly knows our older methods and above all is cognizant with the phenomenal results of radiotherapy, including X-ray though less potent and dependable.

As a rule, most of our carcinoma cases need efficient radiation either to inaugurate or to complete the cure, whatever other adjuvant methods we may adopt. Electrosurgery is often a preliminary to facilitate radiation, serving an excellent purpose in removing and sterilizing a massive disease down to its base to insure a more direct, efficient application of the succeeding therapy. On the other hand it is sometimes well to apply radium first, for its effects act in the more distant peripheral zone, to be followed in a few days by the more localized radical electrosurgery. It is indeed a happy concomitance that both of these agencies are not mutually exclusive but coöperative as they work together to promote the desired result. By and large, be it said, it is rare that a new method coming in wholly displaces the old, but rather does it supplement and increase its effectiveness and enlarge its territory.

# CARCINOMA OF THE PROSTATE\*

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FROM THE UROLOGICAL SERVICE OF THE MEMORIAL HOSPITAL

CARCINOMA of the prostate still holds its place as the most baffling of urological conditions. We know little of its etiology. In but a small percentage of cases is the diagnosis made sufficiently early to give any sort of treatment a fair chance of success. Even if an early diagnosis be made there is no general agreement as to the best way to treat this neoplasm. We hold that the possibilities of radical surgery have been thoroughly exploited while the effective use of radiation is still far from the practical limits of its application to this disease. This paper is written in an attempt to analyze the reasons for the failures of the past, to discuss our present ideas on the subject and to suggest further improvement in the control of the disease by radiation.

*Diversity of Therapeutic Policies.*—Young, who has employed the quite intricate radical operation for cancer of the prostate reports twenty-seven cases, the first in 1904 and the last in 1927,<sup>1</sup> just a little over one a year. This would seem to indicate how very few cases coming to his service are believed to be suitable for radical operation. In a large majority of these cases the diagnosis of carcinoma was made before operation. In a fair percentage the carcinoma had extended beyond the limits of the prostate. In our own experience at the Memorial Hospital less than 5 per cent. of all prostatic cancers were confined to the organ. In Young's series, eight patients of the twenty-seven are reported alive and well for periods varying from three to thirteen years after operation. Young believes that the radical operation should be performed in selected cases. In other cases he does a modified radical operation using radium at the time of or after operation. In certain cases he has used radium alone or in combination with X-ray therapy.

Raymond Dossot<sup>2</sup> after an extensive study of prostatic carcinoma, in 1926, concluded that radiation was better treatment than surgery as being more benign in its application, but stated that the possibilities of radiation had not been fully investigated. At that time he regarded all treatment as palliative only. In a more recent article on the subject<sup>3</sup> he reiterates his pessimism as to any form of therapy except palliation, attacks Young's radical prostatectomy vigorously and sees the best results in cystotomy and palliative radiation.

Young<sup>4</sup> in replying to Dossot's attack on radical surgery states that since the adoption of his recent technic thirty-five radical prostatectomies have been performed for carcinoma of the prostate with but one operative death.

Smith formerly put much faith in Young's operation but more recently<sup>5</sup> seems to have become impressed by the possibilities of deep X-ray therapy for growth restraint. He noted the marked histological changes occurring in a carcinomatous prostate so treated.

Marion and Wildbolz<sup>6</sup> believe that operative removal offers the only chance of control. Wildbolz found forty of 145 patients with prostatic carcinoma suitable for this form of therapy and so treated them.

Bumpus reviewed the cases at the Mayo Clinic in which operation had been undertaken for benign hypertrophy but in which carcinoma had been discovered on routine

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\* In part from the Guggenheim Fund for Urology.

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microscopic examination of the sectioned organ. He believes that the best chance for cure by surgery lies in this group of cases, namely those in which the neoplasm is not clinically demonstrable but proves to have carcinoma on histological section. In a clinical study of 1,000 cases Bumpus<sup>7</sup> states that in many cases the malignant disease was discovered only at operation but when it was also clinically evident the results were poor. He further states that in his opinion the most satisfactory form of treatment is operation followed by radiation.

Chute<sup>8</sup> deals simply with the urinary retention caused by the neoplastic process. He does a partial prostatectomy, repeating it if obstruction recurs with gratifying palliative results. Most urologists believe that partial prostatectomy under these circumstances results in only very temporary control of the urinary retention and prefer the catheter or permanent suprapubic drainage.

*Causes of Failure of Treatment.*—The natural history of prostatic carcinoma presents many obstacles to effective therapy. The protean forms of the neoplastic process, lack of definitive symptomatology, the simulation of benign disease, make early and accurate differential diagnosis difficult. Radical surgery and palliative operations are quite generally conceived and executed with total disregard of the true biologic nature of the problem that must be met. Radiation has also failed to produce the best results, but in its conception it is sound. Effective application of radiation to prostatic carcinoma can only keep pace with the fundamental progress of the science of radiology. To date this form of therapy has been largely empirical in its application to new growths in the prostate. Only of recent years has it become apparent that more accurate methods and nicer adjustment of dosage to the biophysical reactions of normal and neoplastic tissues are productive of superior results. We have already felt the force of these advances and find that their application to the problem in hand has resulted in gradual improvement in the response of these malignant tumors to radiation.

The early local extensions of the disease have been noted with appalling frequency by most observers, yet few seem to appreciate the still greater and earlier incidence of pelvic lymphadenopathy. In Dossot's series<sup>2</sup> metastasis to the regional nodes in the pelvis occurred in 89.4 per cent., while Pasteau, quoted by Dossot, described this event in sixty of seventy-one observations.

A point of still greater importance bearing on the choice of therapy is the early infiltration of the capsule of the organ by the neoplastic process. Before local extension can be appreciated the new growth has frequently invaded the fibromuscular capsule by way of the loose cellular septa, gaining ready access to the small venules of the surrounding prostatic plexus. These veins are rapidly invaded by tumor cells rendering surgical intervention an impossibility without immediate dislodgment of tumor emboli, followed by distant metastasis. While we are not yet armed with the figures we believe that this type of extension occurs as early and with almost as great frequency as does extension by way of the lymphatics and the regional nodes. Certainly both events precede the direct gross anatomical extensions of the disease. The involvement of the capsule in the manner described is often noted by the surgeon when he fails to find a satisfactory "line of cleavage" between gland

and capsule. It also explains the prompt and frequent post-operative recurrences, as few operators are so radical as to remove the last shred of infiltrated capsular tissue along with the entire venous plexus. Nor is this all. We have further evidence of a convincing nature that adenocarcinoma is frequently primary in the accessory prostatic glands at the bladder base, variously termed the subcervical group, glands of Albarran, *etc.*, these tumors later extending into the substance of the prostate proper, fungating through the bladder mucosa, or both. Furthermore, the earliest direct extension of the disease when primary in the true prostate is frequently in the direction of this group of accessory glands. In our material, primary or secondary involvement of this group is more frequent than the time-honored extension to the seminal vesicles.

Pelvic lymphadenopathy occurring in a very high percentage of all cases of carcinoma of the prostate, a high early incidence of capsular infiltration and venous thrombosis by tumor cells, frequent primary or secondary involvement of the accessory glands at the bladder base, all often present when the patient is first compelled to seek advice, constitute an insurmountable barrier to the successful surgical treatment of the disease no matter how radical its conception and execution.

*Age Incidence.*—The age incidence of cancer of the prostate does not differ greatly from that of benign hypertrophy so that this factor alone is of little value in differential diagnosis. Young in a series of 898 cases of benign hypertrophy showed that 794 or 88.4 per cent. occurred between the ages of fifty and seventy-five. In our present series of 280 cases of cancer of the prostate at the Memorial Hospital 197 or 86.6 per cent. fall in the same age group.

TABLE I

*Age Incidence on Admission of Carcinoma of the Prostate in 227 of 280 Cases Studied at the Memorial Hospital*

|                          | Number<br>of cases | Percentage<br>of group |
|--------------------------|--------------------|------------------------|
| Under 34.....            | 1                  | 0.4                    |
| 35 to 39.....            | 3                  | 1.3                    |
| 40 to 44.....            | 3                  | 1.3                    |
| 45 to 49.....            | 6                  | 2.6                    |
| 50 to 54.....            | 26                 | 11.4                   |
| 55 to 59.....            | 42                 | 18.5                   |
| 60 to 64.....            | 44                 | 19.3                   |
| 65 to 69.....            | 50                 | 22.0                   |
| 70 to 74.....            | 35                 | 15.4                   |
| 75 to 79.....            | 13                 | 5.7                    |
| 80 to 84.....            | 3                  | 1.3                    |
| 85 to 89.....            | 1                  | 0.4                    |
| <hr/>                    |                    |                        |
| Total ages 50 to 75..... | 197                | 86.6                   |
| Total entire group.....  | 280                | 99.6                   |

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The peak age group for benign hypertrophy occurs, according to Young, at fifty-five to fifty-nine. The peak age group for cancer in our series is at ages sixty-five to sixty-nine, ten years later. However, this is of academic interest only for the difference for each five-year period is relatively slight. We present a table of age incidence comparing groups reported by various authors with our own experience.

TABLE II  
*Age Incidence of Carcinoma of the Prostate*

| Ages          | Young, 1909<br>111 cases<br>Per cent. | Bumpus, 1921<br>361 cases<br>Per cent. | Deming, 1922<br>100 cases<br>Per cent. | Barringer, 1930<br>280 cases<br>Per cent. |
|---------------|---------------------------------------|--|--|---|
| 40 to 50..... | 1.8                                   | 2.7                                    | 3.0                                    | 3.9                                       |
| 50 to 60..... | 22.5                                  | 21.6                                   | 17.0                                   | 29.9                                      |
| 60 to 70..... | 45.5                                  | 51.2                                   | 45.0                                   | 41.3                                      |
| 70 to 80..... | 27.0                                  | 22.1                                   | 25.0                                   | 21.1                                      |
| 80 to 90..... | 3.6                                   | 1.2                                    | 10.0                                   | 1.7                                       |

The statistics show no marked disagreement but our experience shows a slight increase in the earlier age groups with a corresponding decrease in the later years. However, these are all relatively small series and a truer picture would probably be given by averaging all the figures.

*Symptomatology.*—The symptoms of cancer of the prostate are not easily differentiated from those of benign hypertrophy, for both conditions are often present at the same time. A prostatic carcinoma is frequently superimposed upon a benign hypertrophy but many cancers develop in non-hypertrophied prostates as well. An earlier diagnosis usually is made where the neoplastic process develops subsequent to the benign hypertrophy. It is not surprising that even competent urologists often fail to recognize these superimposed cancers as the true condition is often masked by œdema. Hard carcinomatous nodules are easy to miss when covered by œdematous prostatic tissue. We have found that after subjecting these doubtful or suspicious superimposed cases to a cycle of high voltage X-ray, causing the œdema of the hypertrophied organ to disappear, the diagnosis is easier. Then the hard cancer tissue stands out sharply defined from the elastic enlargement of the benign hypertrophy.

The initial symptoms of carcinoma of the prostate fall into two main groups; 1, urinary symptoms; and 2, pain. The urinary symptoms are usually the first observed by the patient and therefore the most important from the point of view of early diagnosis. The two most common symptoms occurring early in the disease are frequency and difficulty of urination. In 82 per cent. of our 280 cases these two symptoms were the first exhibited. Other common symptoms associated with the above are nocturia, retention, hæmaturia, urgency and incontinence.

The symptoms of pain which cause the patient to consult his physician are, in the order of their importance; painful urination, backache, pain down the thighs and legs ("sciatica"), pain in the lower abdomen and pelvis, pain in

the hips, groin, penis, rectum, and perinæum. Most of these are late symptoms, due to direct invasion of the bladder neck, to pressure on nerve trunks by invaded pelvic nodes, obstruction to the venous circulation from the same cause, or to distant metastases, especially to the bones. We here present a tabulation of the initial symptoms occurring in 280 cases of cancer of the prostate.

TABLE III  
*Initial Symptoms Occurring in 280 Cases of Cancer of the Prostate*

| Symptom                      | Number | Per cent. |
|------------------------------|--------|-----------|
| Frequency.....               | 134    | 47.8      |
| Difficulty.....              | 96     | 34.2      |
| Nocturia.....                | 79     | 28.2      |
| Dysuria.....                 | 60     | 21.4      |
| Retention.....               | 45     | 16.0      |
| Backache.....                | 26     | 9.2       |
| Hæmaturia.....               | 24     | 8.5       |
| Pain in thighs and legs..... | 19     | 7.5       |
| Pain in lower abdomen.....   | 14     | 5.0       |
| Urgency.....                 | 12     | 4.2       |
| Incontinence.....            | 11     | 3.9       |
| Constipation.....            | 10     | 3.5       |
| Pain in hips.....            | 9      | 3.2       |
| Loss of weight.....          | 8      | 2.8       |
| No urinary symptoms.....     | 8      | 2.8       |

Usually patients presented three or more symptoms at the onset, which caused them to consult a physician. The most common triad was that of frequency, difficulty and nocturia. Many patients waited, however, until retention or hæmaturia compelled them to seek advice. Retention in itself is not indicative of far-advanced cancer. It is often caused by associated benign hypertrophy. Diligent search for carcinomatous changes in the prostate of the retentive case will often lead the surgeon to an early diagnosis of prostatic carcinoma. Many of our patients' histories indicate the possibility of much earlier diagnoses had their physicians made careful digital examinations at the time of the first attack of retention. In our series, an average of twenty-four months had elapsed between the appearance of initial symptoms and our first examination. Hæmaturia, on the other hand, is seldom an early symptom, usually occurring only when the tumor has invaded the posterior urethra or bladder. Twenty-four or 8.5 per cent. presented hæmaturia as the initial symptom and thirty-nine or 13.9 per cent. as a subsequent symptom. Hence a total of sixty-three had hæmaturia at some time in the course of the disease, cystoscopic examination proving forty-one of these to have extension of the neoplastic process to the bladder.

Occasionally there are no urinary symptoms in well-advanced cases of prostatic cancer, as in eight of our patients. In these eight the symptoms were referred to the gastro-intestinal tract and the genital organs. One consulted his physician because of persistent diarrhœa. Another because of

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rectal bleeding for which he was subjected to hæmorrhoidectomy, the true nature of his disease becoming apparent only after the failure of the operation to relieve his symptoms. A third complained of curved erections of the penis over a period of three years, due to direct invasion of the corpora by prostatic cancer. The fourth had a colostomy and later a resection for supposed rectal carcinoma before the tumor was shown to be of prostatic origin. In a fifth, resection of the right ileum was undertaken for a new growth which proved to be a metastasis from a cancerous prostate. The sixth and seventh suffered operative attacks on various metastatic lesions of the disease, while the last complained of incontinence of fæces due to invasion of the sphincter ani by the tumor.

The later symptoms of cancer of the prostate do not differ greatly from the initial symptoms. Urinary symptoms and pain are the most important, nocturia, retention and hæmaturia leading the list. A tabulation of these and other later symptoms in our series of 280 cases follows:

TABLE IV  
*Secondary Symptoms Occurring in 280 Cases of Cancer of the Prostate*

| Symptom                      | Number | Per cent. |
|------------------------------|--------|-----------|
| Nocturia.....                | 51     | 18.2      |
| Retention.....               | 45     | 16.0      |
| Hæmaturia.....               | 39     | 13.9      |
| Frequency.....               | 34     | 12.1      |
| Dysuria.....                 | 32     | 11.4      |
| Loss of weight.....          | 31     | 11.0      |
| Backache.....                | 25     | 8.9       |
| Loss of strength.....        | 20     | 7.1       |
| Pain in thighs and legs..... | 18     | 6.4       |
| Pain in lower abdomen.....   | 14     | 5.0       |
| Constipation.....            | 13     | 4.6       |
| Rectal pain.....             | 10     | 3.5       |

Less frequent symptoms occurring late in the disease referred chiefly to the incidence of distant metastases or to regions unrelated to the urinary tract.

*Early Diagnosis and Biopsy.*—It seems superfluous to state that earlier diagnosis is of prime importance, yet with twenty-four months on the average elapsing between the onset of symptoms and the establishment of the diagnosis in the patients represented in this series, the point can stand vigorous emphasis. We<sup>9</sup> have stressed previously the importance of routine examination of the prostate in all men over fifty years of age. We would now add that the persistent exhibition of frequency, difficulty in urination, nocturia and retention in any patient of cancer age calls for a most careful and painstaking search for prostatic carcinoma.

The difficulties of accurate diagnosis of prostatic neoplasms have been considerably decreased by the adoption of biopsy by needle puncture and aspiration according to the technic of Martin and Ellis<sup>10</sup> and applied to the prostate by one of us.<sup>11</sup>



In the series of cases here reported, 280 in number, there was histological confirmation of the clinical diagnosis by some form of biopsy or surgical specimen in forty-nine. This represents 17.5 per cent. of the total. Since the addition of biopsy by needle puncture and aspiration to our routine examination, except in those cases going to operation, we have secured histological evidence of our diagnosis in fourteen of the fifteen cases admitted. In five the specimen was obtained by Young's punch, while in nine the tissue was secured by our new biopsy technic. In one case no attempt at biopsy was made. Moreover, biopsy by aspiration has enabled us to secure important information in several older cases. In one a recurrence after four years of

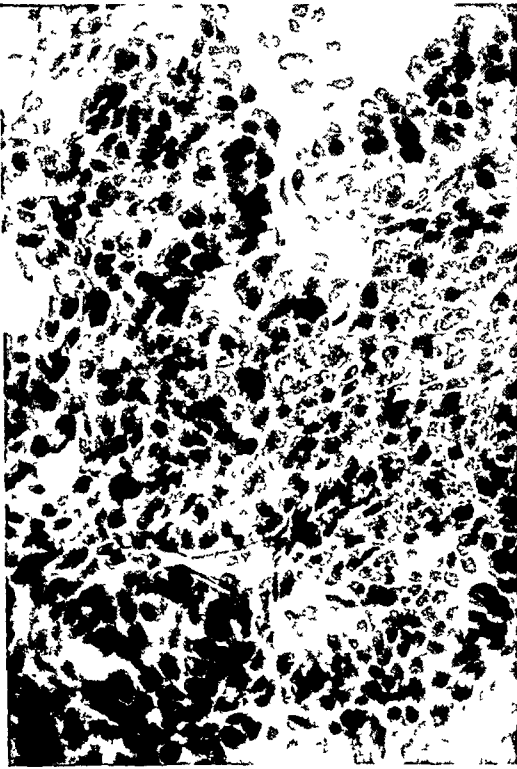


FIG. 1.—Specimen of tissue aspirated from far-advanced adeno-carcinoma of the prostate.



FIG. 2.—Specimen aspirated from small recurrent nodule. Adeno carcinoma of the prostate under apparent control by radiation four years.

apparent control was proven; in another previously regarded as chronic interstitial prostatitis a carcinoma was demonstrated. Among the more recent cases, this form of biopsy enabled us to make a diagnosis of cancer in two early cases previously regarded as benign. In another a rare prostatic tumor was diagnosed in advance, and later proven at operation, by means of this procedure. Figs. 1 to 4 illustrate some of the above-mentioned cases together with the amount and character of the tissues obtained by needle puncture and aspiration. If we are seeking earlier diagnoses of these tumors it must be recognized that carcinoma may and does originate in any portion of the organ, regardless of the presence or absence of benign hypertrophy, and that no false sense of security should be felt due to apparent normality of the posterior

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lobe. By utilizing this advance in biopsy technic any suspicious nodule in the prostate may be readily subjected to microscopic study.

*Treatment by Radiation.*—A review of the use of radium and X-rays in carcinoma of the prostate at the Memorial Hospital reveals the difficult situation we are called upon to meet. An estimate of the status of 241 of the 280 cases here reported, made at the time of our first examination in each case, shows that 221 were classified as advanced cases while only twenty could fairly be classed as early cases. Seventy-eight of the 221 represented post-operative recurrences.

In spite of the far-advanced type of case coming to our service, we were



FIG. 3.—Small cell adeno-carcinoma of prostate. Clinical diagnosis difficult, proven by aspiration biopsy.

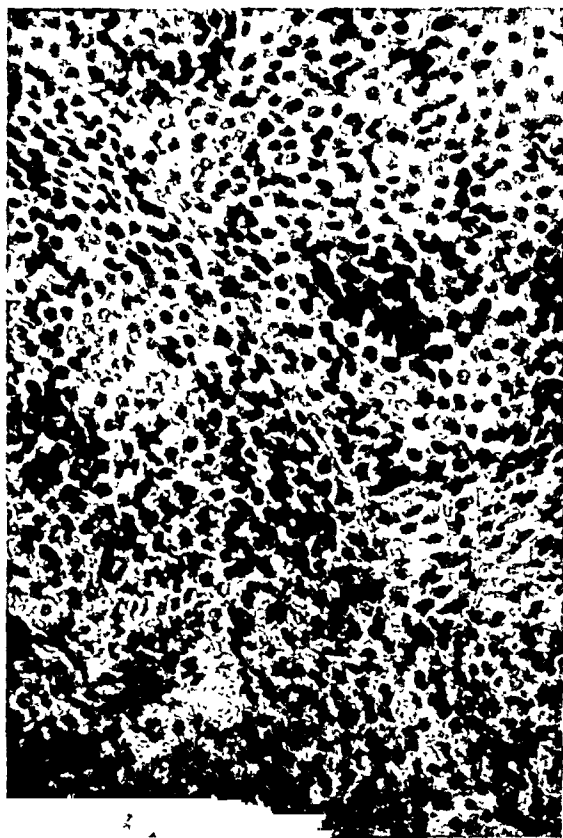


FIG. 4.—Adeno-carcinoma of the prostate. Early clinical case at first regarded as benign. Proven carcinoma by aspiration biopsy.

able to report five of forty-six cases alive and well after five years.<sup>12</sup> These forty-six patients constituted our first series and were treated between October, 1915, and January, 1917. In but one case was the neoplastic process confined to the prostate. No gross evidence of active cancer remained in the five patients surviving the five-year period, as far as we could see. These cases were treated by the insertion of steel radium-bearing needles through the perinæum into the prostate and seminal vesicles. Small doses, 200 to 300 millicurie hours for each needle, were utilized, repeating the dose every two to three months until the condition was controlled or no evidence of regression was found. In this way we were certainly able to control some cases as we have the autopsy record of one patient in this group who died from other

causes seven years after first seen. The original tissue diagnosis by Doctor Ewing was carcinoma of the prostate. At autopsy no carcinoma was to be found.

Since that first series progress has been slow but sure. Our therapeutic routine has had to be changed frequently in order to avail ourselves of the advantages of newer methods and agents. Glass seeds of radon, low voltage and then high voltage X-rays, the radium element pack, radon filtered by platinum and now gold seeds of radon have all been used alone and in various combinations. We are gratified, however, that in spite of the necessity for the continual transition of radiation therapy, inspection of our file of current cases shows eight of forty patients alive and well for periods over five years. This means that 20 per cent. of our active cases are still under control after five years as compared with 10.8 per cent. in our first reported series.

We believe that in most cases of prostatic carcinoma a much larger dose of radium than heretofore used is necessary to control the disease. In other words, doses comparable to those we have used in controlling bladder carcinoma. The results of radium implantation in bladder tumors have consistently improved and are considered by us to be quite superior to operative resection.

We believe that a tissue dose of somewhere between 10 and 15 skin erythemas delivered to the tumor is necessary to control the large majority of prostatic carcinomata. The average adenocarcinoma is a radio resistant tumor but doses comparable to the above are sufficient for control in other locations and will undoubtedly prove so in cancer of the prostate. Since tissue dosage delivered to these tumors by external means alone, *i.e.*, high voltage X-rays and the radium element pack, can rarely exceed 1 to 1½ S.E.D., it becomes essential to deliver the bulk of the total dose necessary by interstitial radiation with gold seeds of radon. Because of this necessity for a large dose of radon accurately placed within the prostate we have quite reversed our original contention that the best approach was through the perinaeum. We believe that cystotomy should be done, any obstructive portions of the prostate removed with cutting forceps or cautery, and the entire tumor, no matter what its limits, implanted with radon using seeds of 2 millicuries each to every cubic centimetre of new growth. In this way we are able to use doses adequate to the need, at the same time making the patient more comfortable and avoiding the risk of renal decompensation due to obstruction at the bladder neck. It seems to us that the suprapubic exposure is better suited to the purpose than the perineal route as that region is allowed to remain intact, securing its value as a protective barrier to tumor extension.

#### SUMMARY

There is no general agreement among urologists as to the best therapy for carcinoma of the prostate.

It is held that the possibilities of radical surgery are exhausted, certain

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features in the natural history of the disease precluding the effective application of this form of treatment.

It is shown that there has been gradual improvement in the control of carcinoma of the prostate by radiation.

The age incidence and symptoms displayed in a series of 280 cases of carcinoma of the prostate are tabulated.

The early diagnosis of the disease is discussed and the use of a new biopsy technic is suggested.

Treatment by radiation is discussed. Higher tissue doses and cystotomy are believed essential to the more effective control of prostatic carcinoma.

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# SOME COMMONER DIFFICULTIES IN DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE RECTUM AND COLON

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THIS discussion is based upon an analysis of 224 cancers of the rectum and colon, collected through the Cancer Division of the Department of Health of the City of Detroit.† It represents practically all of the cases treated in the Detroit hospitals for a period of two years and two months—May, 1927, to July, 1929. In addition, thirty-six cases of cancer of the colon, collected from the University of Michigan Hospital records\* are added, making a total of 260 cases.

Data of this sort do not always lend themselves to an accurate analysis of symptoms, and the scattered auspices under which treatment was carried out does not lead to constructive analysis of methods. Neither of these was attempted. This study has been concerned with the commoner difficulties in early diagnosis; the early symptoms recorded on the hospital charts; the difficulties in X-ray diagnosis; a brief exhibit of treatment; and some of the problems in treatment as shown by these records.

The 224 cases collected from Detroit hospitals include, with a few possible exceptions, the entire experience of the hospitals in Detroit for two years and two months in cancers of the colon and rectum. During this time 350 persons were registered as having died of cancer of the colon and rectum, so that those treated in hospitals represent 65 per cent. of the total deaths (Table I).

TABLE I  
*Number of Cancers of Colon and Rectum Studied*

|                                | Detroit hospitals | Univ. Hosp., Ann Arbor | Total |
|--------------------------------|-------------------|------------------------|-------|
| Rectum.....                    | 73                | 0                      | 73    |
| Rectosigmoid.....              | 32                | 8                      | 40    |
| Sigmoid.....                   | 46                | 11                     | 57    |
| Descending colon.....          | 10                | 3                      | 13    |
| Splenic flexure.....           | 6                 | 3                      | 9     |
| Transverse colon.....          | 14                | 6                      | 20    |
| Hepatic flexure.....           | 10                | 2                      | 12    |
| Cæcum and ascending colon..... | 21                | 3                      | 24    |
| Colon.....                     | 8                 | 0                      | 8     |
| Appendix.....                  | 4                 | 0                      | 4     |
| Total.....                     | 224               | 36                     | 260   |

\* For the privilege of using these records, we are indebted to Dr. Frederick A. Collier, Director of Surgery, University Hospital, Ann Arbor, Michigan.

† Through the courtesy of Dr. Chas. E. Dutchess, Director.

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Tables II and III contrast the Detroit hospital's incidence of rectum and colon cancer with the incidence as obtained from death certificates over a period of two and one-half years. For comparison, the incidence over five years at the University Hospital, Ann Arbor, is given.

It shows:

(1) Hospital incidence in Detroit agrees quite well with death-certificate incidence, except in the percentage of rectosigmoid growths and transverse colon, both of these being greater in the hospital series. The death certificates had 25 per cent. unclassified cases (death due to cancer of the colon, exact anatomical site not determined), compared to  $3\frac{1}{2}$  per cent. in hospital cases.

(2) The table from Ann Arbor shows a very high comparative incidence of rectal cancers. Perhaps the reason is that these cases, since they do not so generally develop obstruction, are more apt to be able to travel.

TABLE II

*Carcinoma of Colon and Rectum. IIospital Incidence Compared to Death Certificate Incidence*

|                               | Deaths—Detroit<br>Department of<br>Health—3 years,<br>1927-28-29 |           | Detroit hospitals—<br>2½ years |           | University<br>Hospital,<br>Ann Arbor—<br>5 years |           |
|-------------------------------|--|-----------|--------------------------------|-----------|--|-----------|
|                               | No.  | Per cent. | No.                            | Per cent. | No.  | Per cent. |
| Rectum.....                   | 125  | 33.9      | 73                             | 32.6      | 138  | 62.4      |
| Rectosigmoid.....             | 13   | 3.6       | 32                             | 14.3      | 5  | 2.2       |
| Sigmoid.....                  | 77   | 20.9      | 46                             | 20.5      | 29   | 13.1      |
| Descending colon.....         | 6  | 1.6       | 10                             | 4.5       | 8  | 3.6       |
| Splenic flexure.....          | 5  | 1.4       | 6                              | 2.7       | 5  | 2.3       |
| Transverse colon.....         | 10   | 2.7       | 14                             | 6.2       | 7  | 3.2       |
| Hepatic flexure.....          | 7  | 1.9       | 10                             | 4.5       | 1  | 0.5       |
| Cæcum and ascending colon.... | 33   | 8.9       | 21                             | 9.4       | 17   | 7.7       |
| Colon.....                    | 91   | 24.8      | 8                              | 3.5       | 11   | 5.0       |
| Appendix.....                 |  | .3        | 4                              | 1.8       | 0  | 0.0       |
| Total.....                    | 367  | 100.      | 224                            | 100.      | 221  | 100.      |

TABLE III

*Incidence*

|                   | Death<br>certificate—<br>Department of<br>Health—3 years | Detroit<br>hospitals | University<br>Hospital,<br>Ann Arbor | Yoemans<br>series |
|-------------------|--|----------------------|--------------------------------------|-------------------|
| No. of cases..... | 215  | 151                  | 172                                  | 88                |
| Rectum.....       | 58.1   | 48.3                 | 80.3                                 | 31.8              |
| Rectosigmoid..... | 6.0  | 21.2                 | 2.9                                  | 22.7              |
| Sigmoid.....      | 35.9   | 30.5                 | 16.8                                 | 45.5              |

Table III shows the per cent. incidence estimated for rectum, rectosigmoid and sigmoid only, with a table from Yoeman's Proctology\* for comparison. Evidently, from these two tables, there are fewer rectosigmoid cancers re-

\* Yeoman's Proctology. Appleton, p. 498, 1929.

ported in death certificates than one should expect from the hospital incidence of growths in this anatomical site. The reason is not clear.

#### SYMPTOMS

Of the 260 cases, information concerning the duration of symptoms before diagnosis, the first symptoms complained of, and whether or not there was obstruction at the time of operation (or diagnosis) was obtained in 213. These are charted in Table IV. These cases came to operation from 6–12 months after the onset of symptoms; the shortest being splenic flexure, 5.9 months, the longest, rectosigmoid, 13.2 months. At the time of operation (or diagnosis) 40–75 per cent. showed obstruction, either chronic or acute (excepting rectal and cæcal growths, where obstruction is not prominent). As will be noted later, this is much too late for good results from treatment. All are agreed that earlier recognition would contribute more to better results than any other factor. Hence the importance of early, or first symptoms.

*Rectum.*—It is evident that, in this series, bleeding from rectum—the commonly known symptom of rectal cancer, was noted as the first symptom in only one-third of the cases. The usual rectal carcinoma is the adenocarcinomatous ulcer in the ampulla. Following a symptomless period during which the tumor must be small, there is a well-recognized stage during which symptoms are chiefly tenesmus, pain, or discomfort in the region of the rectum. It is only later, when ulceration develops, that bleeding takes place. Almost half of these cases started with tenesmus, pain in the rectum, or diarrhœa (sometimes bloody or blood streaked, but chiefly diarrhœa). Bleeding (except as blood-streaked diarrhœa in which the diarrhœa was the patient's chief complaint) was generally noted as starting 1–3 months after these symptoms of rectal irritation. A few started with increasing or suddenly appearing constipation, a few with the sensation of a mass. Gas in the bowel—distention—is not a very common symptom of the onset of rectal cancer. Often where this was noted as the initial symptom, further study showed the anatomical location to be the rectosigmoid junction or sigmoid rather than the rectum proper.

From our records, it is doubtful whether these pre-ulcer symptoms are generally looked upon by either the patient or the attending physician as of possible serious significance. The cases, however, seem to be recognized in the bleeding stage. Very few were noted as having obstruction. We have records of only two cases where hæmorrhoidectomy was done (both by medical irregulars), and two others where medical treatment was given during the time in which the patient had symptoms of cancer.

*Rectosigmoid.*—Here one-fourth started with rectal bleeding as the first symptom. About half started with symptoms of constriction: obstinate constipation (either from previous mild constipation or from previous health), or symptoms of irritation—diarrhœa, alternating diarrhœa and constipation, tenesmus, etc. The remainder started with left lower abdominal pain, loss of weight and weakness, etc. Blood was usually present in the stools after

## TABLE VIII

| Total number | Per cent. obstruction at time of diagnosis or operation | Average duration symptoms before diagnosis, mos. |                                | Bleeding | Diarrhoea | Pain in rectum, bearing down pain, tenesmus, etc. | Obstinate constipation | Mass in rectum | Alternating constipation and diarrhoea | Lower abdominal pain | Subacute or acute obstruction | Right lower quadrant pain | Loss of weight, or weak | Mass in abdomen | Pain in back | No symptoms |
|--------------|---|--|--------------------------------|----------|-----------|---|------------------------|----------------|--|----------------------|-------------------------------|---------------------------|-------------------------|-----------------|--------------|-------------|
| 66           | .0  | 9.1  | Rectum.....                    | 23       | 13        | 15  | 7                      | 3              | 2                                      | 3                    | 1                             | 1                         | 4                       |                 | 1            | 1           |
| 30           | 41.6  | 13.2   | Rectosigmoid.....              | 8        | 5         | 1   | 6                      |                |  | 3                    | 1                             |                           |                         |                 |              |             |
| 43           | 60.8  | 7.2  | Sigmoid.....                   | 6        | 2         | 1   | 8                      |                |  | 13                   | 2                             |                           | 4                       |                 |              |             |
| 12           | 41.6  | 11.7   | Descending colon.....          | 3        |           |   | 5                      |                |  | 3                    | 9                             |                           |                         |                 |              |             |
| 9            | 77.1  | 5.9  | Splenic flexure.....           |          |           |   | 1                      |                |  | 3                    | 2                             |                           |                         |                 |              |             |
| 19           | 68.4  | 11.1   | Transverse colon.....          |          | 1         |   | 1                      |                | 2                                      | 4                    | 1                             |                           |                         |                 |              |             |
| 11           | 60.   | 9.4  | Hepatic flexure.....           |          |           |   |                        |                | 1                                      | 13                   |                               | 1                         | 2                       |                 |              |             |
| 19           | 12.5  | 11.2   | Cecum and ascending colon..... |          |           |   | 1                      |                |  | 6                    |                               | 2                         |                         | 2               |              |             |
| 4            | .0  | 8.3  | Appendix.....                  |          |           |   |                        |                |  | 5                    |                               | 11                        |                         | 2               |              |             |
| 213          |   |  | Total.....                     | 42       | 21        | 17  | 29                     | 3              | 5                                      | 51                   | 14                            | 17                        | 10                      | 2               | 1            | 1           |

# Comparison of Recoveries and Post-operative Deaths from Resections of the Rectum and Colon for Cancer

| Recovery   |                      |                        |                       |             |                           |        | Death                            |        |                           |             |                       |                        |                      |                                 |
|--|----------------------|------------------------|-----------------------|-------------|---------------------------|--------|----------------------------------|--------|---------------------------|-------------|-----------------------|------------------------|----------------------|---------------------------------|
| Fixation; extension; metastases at time of operation | Second stage removal | Resection, first stage | Preliminary colostomy | Obstruction | Average duration symptoms | Number | Resections                       | Number | Average duration symptoms | Obstruction | Preliminary colostomy | Resection, first stage | Second stage removal | Metastases at time of operation |
| 11   | 7                    | 9*                     | 7                     | 0           | 5.8                       | 16     | Rectum.....                      | 14     | 8                         | 0           | 5                     | 9†                     | 5                    | †                               |
| 0  | 2                    | 2                      | 1                     | 1           | 20                        | 4      | Rectosigmoid.....                | 5      | 18                        | 3           | 1                     | 3                      | 1                    | 2                               |
| 3  | 4                    | 1                      | 1                     | 4           | 12                        | 6      | Sigmoid.....                     | 16     | 6.4                       | 11          | 7                     | 8                      | 7                    | 3                               |
| 2  | 0                    | 4                      | 0                     | 2           | 8                         | 4      | Desc. splenic; trans. colon..... | 7      | 5                         | 1           | 0                     | 7                      | 0                    | 1                               |
| 1  | 2                    | 1                      | 3                     | 1           | 7                         | 4      | Ileopatic; caecum.....           | 7      | 6.5                       | 1           | 2                     | 4                      | 1                    | 3                               |
|  |                      |                        |                       |             |                           | 34     | Total.....                       | 49     |                           |             |                       |                        |                      |                                 |

\* Perineal resections.  
† Five abdominal perineal, four perineal resections.  
‡ Not definite.



the lesion had existed for 2-3 months and there was a frequent note of subsequent gaseous distention, lower abdominal distress, *etc.*, but not necessarily of symptoms of obstruction.

*Sigmoid and Descending Colon.*—Here lower abdominal pain and distress, and obstinate constipation are the predominating first symptoms. Of fifty-five cases of both sigmoid and descending colon, sixteen started with abdominal pain and distress—sometimes mild bloating, sometimes sharp colicky attacks; thirteen with obstinate constipation and eleven with attacks of subacute or acute obstruction. Of the remaining fifteen, eleven started with rectal symptoms—bleeding, diarrhoea, tenesmus, *etc.*—and the remainder (four) with loss of weight and weakness. Evidently the abdominal pain is not always suspected of being due to sigmoid cancer. It was described as vague dyspepsia and abdominal distress simulating an upper abdominal lesion just as often as “lower abdominal pain.” Only occasionally was it noted as pain to the left of the umbilicus. The majority of these sigmoid growths which started with vague pain or obstinate (or increase in) constipation, shortly developed attacks of subacute obstruction. As noted, eleven started with attacks of suddenly appearing obstruction. Several cases gave histories of such attacks, with distention and sometimes vomiting for 3-5 months before the diagnosis was made. In some cases patients were admitted to hospitals, then discharged in a few days after the attack subsided.\* One case had an operation for inflammatory disease of the adnexa during the course of the symptoms. As noted, blood in the stools is a less frequent early warning than is the careful investigation of lower abdominal pains. When present, of course, it is definite. All authorities mention its early importance. The charts also left the impression that earlier local examination by proctoscopy and sigmoidoscopy would be of considerable value.

*Splenic Flexure, Transverse Colon.*—The symptoms here are similar. Blood in the stools ceases to be an early symptom after the splenic flexure is passed, and the abdominal distress is of most importance. It was described as flatulent bloating, lower or general abdominal pains and distress, cramps in the abdomen or severe colicky pains. The importance of careful anamnesis is great—for 60-80 per cent. of these cases have obstruction when they finally come to operation, and the early symptoms, probably due to spasm of the bowel at the site of constriction, are regularly unrecognized. In a few cases, a so-called phantom tumor was felt, which disappeared immediately, giving a false sense of security. Subsequent events showed that these were probably faecal impactions proximal to the site of constriction, and as the oedema, *etc.*, at this site subsided, the tumor disappeared. The colon can accommodate itself to marked degrees of narrowing and produce only very mild symptoms. A diet for spastic constipation may give complete relief. Alvarez records a patient who lived for years in relative comfort on a bland diet, with an unus-

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\* “It is rather disturbing to find patients being sent out from hospitals because the X-ray shows no lesion, and in spite of the fact that there is a typical history of cancer of the colon or rectum . . .” Jones, Daniel F.: *ANNALS OF SURGERY*, vol. xc, No. 4, p. 675, October, 1929.

pected stricture of the colon, then suddenly developed acute obstruction with perforation when a small bit of lettuce lodged in the narrowed area. In two cases, abdominal pain caused by early malignant strictures were so mild or atypical as to be diagnosed intestinal flu.<sup>3</sup>

*Hepatic Flexure, Ascending Colon, Cæcum.*—The early pains due to carcinoma at the hepatic flexure were not so frequently confined to the right side of the abdomen as one would think; six complained of lower abdominal pain, two of right lower quadrant pain. Obstruction is not so prominent; the growths attain large proportions, and are sometimes confused with gall-bladder disease—symptomatically, on examination and by röntgenography.

The pain in cæcal and ascending colon growths was chiefly confined to the right lower quadrant. In two cases the first symptom was a mass suddenly appearing on the right side.

Appendectomy was done during the course of the symptoms once for cæcal cancer, once for hepatic flexure and once for transverse colon growths. One case was operated upon for ovarian cyst and a cancer in the region of the cæcum discovered.

In summary, some of the problems in the early recognition of rectal and colon cancers, as revealed by this brief study of 260 cases collected in an average manner are:

(1) Perhaps two-thirds of all rectal cancers have an early period in which symptoms are chiefly tenesmus, pain on defecation, ache in lower sacral region, *etc.*, before there is blood in the stools. This is not generally recognized.

(2) In growths of the colon proper, patients had lower abdominal distress, ranging from mild flatulence with or without nausea to severe colic, for several months before diagnosis.

(3) Several patients had attacks of subacute obstruction for months before cancer of the colon which caused them was recognized.

(4) At the time of diagnosis or operation, 60–80 per cent. of splenic flexure and transverse colon growths were obstructed; 40–60 per cent. of the hepatic, descending, and sigmoid and rectosigmoid. Ascending and rectal growths showed very little obstruction.

(5) A few rectal cancers had hæmorrhoidectomy or medical treatment for hæmorrhoids, a few right colon growths had appendectomy during the course of symptoms. From these records the number is probably less than the usually reported 10–15 per cent.

*X-ray.*—There is a tendency, especially in the average practice of medicine, to attach considerable importance to an X-ray examination. The clear visual picture, the typewritten report, are certainly more demonstrative than the painstakingly obtained history of vague abdominal distress, which often depends for its accuracy upon “that delicate adjustment between a nervous patient’s recital of symptoms and a physician’s powers of analysis.” The

\* Starr, Frederick N. G. (ANNALS OF SURGERY, vol. xc, No. 4, p. 687, October, 1929), remarked that during 1928 he had seen twelve patients with cancer of the rectum and colon “who dated their ill health to an attack of what had been called ‘intestinal flu.’”

fact that the röntgenogram is only a shadow, subject to certain limitations in the demonstration of physiological and pathological processes, may perhaps be worthy of repetition.

Table V shows the total number of cases studied, the number who had no X-ray, and those where there was no note of X-ray examination, in the first three columns. The next three columns show the number of positive X-ray diagnoses, negative reports, and an interesting group in which the X-ray was indefinite or indeterminate. The last column records the percentage of the total number examined in which X-ray was negative or indeterminate. Rectal cancers are not included, since few X-ray examinations were made of these cases.

TABLE V  
*X-Ray Examinations*

|                                   | Total<br>No.<br>studied | No X-ray | No note | X-ray<br>positive | X-ray<br>negative | X-ray<br>indeter-<br>minate | Per cent.<br>X-ray<br>negative<br>and inde-<br>terminate |
|-----------------------------------|-------------------------|----------|---------|-------------------|-------------------|-----------------------------|--|
| Rectosigmoid.....                 | 39                      | 9        | 9       | 17                | 2                 | 2                           | 19.0   |
| Sigmoid.....                      | 51                      | 10       | 12      | 25                | 1                 | 3                           | 13.8   |
| Descending colon.....             | 12                      | 1        | 0       | 10                | 1                 | 0                           | 9.1  |
| Splenic flexure.....              | 9                       | 1        | 1       | 5                 | 1                 | 1                           | 28.6   |
| Transverse colon.....             | 19                      | 2        | 4       | 9                 | 0                 | 4                           | 30.8   |
| Hepatic flexure.....              | 12                      | 0        | 3       | 5                 | 0                 | 4                           | 44.4   |
| Cæcum and ascending<br>colon..... | 20                      | 3        | 4       | 10                | 2                 | 1                           | 23.1   |
| Appendix.....                     | 4                       | 3        | 0       | 0                 | 0                 | 1                           | .....  |
| Total.....                        | 166                     | 29       | 33      | 81                | 7                 | 16                          | 22.1   |

In this series there is an error of 22 per cent. in X-ray examinations, *i.e.*, in that number of proved cancers of the colon and rectosigmoid the X-ray was either negative or indeterminate. A greater percentage of error was made in hepatic—transverse—splenic flexure growths than in descending and ascending colon tumors. In most of the reports where indeterminate diagnoses were given, a spasm or irregular filling defect was noted—sometimes present on one examination, absent on another. In one or two cases, this spasm was present above the tumor in one examination and below in another, the region of the tumor showing no change. This corresponded with palpable tumors present at one time and not at another. Sometimes the delay in stomach and small bowel was noted, but the interpretation was that it was due to a lesion other than carcinoma of the colon—"pancreatic neoplasm"—"obstruction in small bowel," etc.

Two hepatic flexure growths were thought to be more diffuse than cancer—probably tuberculosis or diverticulitis. Another confusion lay in interpreting a smooth walled appearance of the colon, with absence of haustrations, as due to ulcerative colitis, when this flattening was due to the constriction of a growth higher up, which itself could not be demonstrated. All these difficulties probably are due to the fact that the colon very frequently can accommodate itself to quite marked narrowing of its lumen, and still allow the

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passage of the normal faecal current. They are errors in the method, which must be appreciated—the barium shadow can show only the function at the time of examination and is not a mirror of the entire pathological physiology of the bowel.

Another source of confusion lies in the fact that the early symptoms which may denote subacute large bowel obstruction—gas, bloating after meals, distention, *etc.*—passing off without much actual pain, frequently simulate distress due to chronic cholecystitis. An X-ray examination showing a non-filling gall-bladder gives a sense of security; the diagnosis of a comparatively mild intra-abdominal condition contributing to delay in treatment. In two cases X-ray of the gall-bladder only was ordered. In one of these gas in the small bowel was noted—shown at operation to be due to cancer of the cæcum.

The negative and indeterminate X-rays are detailed in Table VI.

TABLE VI

### *X-Ray Indeterminate*

|                               |  |
|-------------------------------|--|
| Rectosigmoid<br>127151        | X-ray.—Slight irregular rectosigmoid spasm or extragastric pathology. Medical diagnosis.—Hodgkin's disease or cholecystitis. Proctoscopic examination.—Cancer rectosigmoid. Operation.—Inoperable cancer rectum.   |
| 2028                          | X-ray.—Ulceration at junction of descending colon and sigmoid. Operation, also proctoscopy.—Mass size fist at rectosigmoid.  |
| Sigmoid<br>142531             | X-ray.—Spasm rectosigmoid junction. No organic pathology. Operation.—Colostomy for cancer sigmoid.   |
| 214533                        | Fluoroscopic negative. First films show constriction, second barium enema negative, third enema adhesions or neoplasm narrowing sigmoid. Medical diagnosis.—Duodenal ulcer. Another X-ray also thought duodenal ulcer. Operation.—Cancer sigmoid.  |
| 158950                        | X-ray.—Questionable defect lower sigmoid. "Believe spastic rather than organic." Operation.—Cancer sigmoid.  |
| Splenic<br>124366             | X-ray defect seen first in transverse colon, then at a second examination seen in descending colon. At operation no tumor found. Colostomy for supposed colitis. Post-operative treatment.—Colitis. Death five and one-half months later. Autopsy.—Cancer splenic flexure.                       |
| Transverse<br>Colon<br>201832 | X-ray inconclusive. Irregular filling defect not constant. Medical diagnosis vitamine deficiency. Autopsy.—Cancer transverse colon.  |
| 2333                          | X-ray.—"While appearance still not typical of malignancy, we think there are indications for laparotomy." Operation.—Typical constricting cancer transverse colon found.   |
| 3335                          | X-ray.—Non-descent cæcum. Delay in small bowel. Partial obstruction in small bowel. At operation.—Annular cancer transverse colon. Microscopic.—Adenocarcinoma.  |
| 2329                          | X-ray in 1925, seventeen months before operation, taken because of belching gas, diagnosed gall-stones. Operation, 1927.—Obstruction mid-transverse colon. Carcinoma.  |
| Hepatic<br>2341               | "While at first we thought there was a definite cancer at right end of transverse loop of colon, repeated examinations make us consider a varying process such as diverticulitis or tuberculosis. Second X-ray against cancer—in favor of tuberculosis. Operation.—Large cancer hepatic flexure. |

|                          |   |
|--------------------------|---|
| 2342                     | X-ray.—Chronic obstruction hepatic flexure. Infiltrating lesion, probably old tuberculosis. Operation.—Large mass upper right, which proved to be cancer of hepatic flexure.  |
| 2317                     | X-ray.—Entire colon normal caliber. No haustration—may be due to ulcerative colitis. Non-filling gall-bladder. Operation.—Massive hepatic flexure cancer. No microscopic.   |
| 2343                     | X-ray.—Redundancy in descending colon, probably due to mucous colitis of large bowel. Slight erosion of the duodenal cap suggests ulcer. Second examination one week later: constriction in sigmoid suggests new growth in this region. Operation.—Cylindrical obstructing cancer at hepatic flexure.                           |
| Cæcum<br>971             | Gastro-intestinal X-ray. Narrowing of transverse colon five inches from hepatic flexure, 1 inch in length, may be due to adhesions or probably cancer. Barium enema, partial obstruction at the point just distal to hepatic flexure. Diagnosis undetermined; does not look like cancer. Operation.—Resection for cancer cæcum. |
| 551                      | Films of gall-bladder show marked gaseous distention of cæcum, ascending and transverse colon with some gas; also seen in terminal loops of ileum. No evidence of gall-stone shadows. Operation.—Appendiceal abscess, possible malignancy. Pathological.—Advanced adenocarcinoma. X-ray negative.                               |
| Rectosigmoid<br>1351     | Gastro-intestinal. X-ray negative. Stomach, duodenal ulcer, small bowel. Operation one month later.—Large mass posterior wall recto-sigmoid junction.   |
| 190588                   | X-ray absolutely negative. Patient died two months later. Autopsy.—Cancer rectosigmoid.   |
| Sigmoid<br>2118          | X-ray.—No definite lesion in colon present. Operation.—Sigmoid adherent in pelvis and contained a carcinomatous mass size of a lemon.   |
| Descending colon<br>1370 | X-ray.—Constriction sigmoid, but on repeated examination after atropin no deformity was noted. One month later acute obstruction. Operation.—Annular cancer sigmoid. Autopsy.—Annular cancer descending colon.  |
| Splenic flexure<br>2320  | Cancer colon suspected clinically. X-ray, no growth. Operation for acute appendicitis nineteen months later. Malignancy splenic flexure found.  |
| Cæcum<br>2350            | X-ray.—Marked twenty-four-hour gastric retention not explained by lesion in stomach, but from pressure from without—might result from cancer of pancreas. Forty-eight hours later there is still a gastric residue. Large bowel well outlined. No defects in colon. Autopsy.—Cancer cæcum.                                      |
| 500x                     | X-ray.—Obstruction pylorus—complete—suggests pancreatic neoplasm. Autopsy three or four days later—ileocæcal cancer.  |

## TREATMENT\*

Table VII lists the treatment of all cases with recovery and deaths of those operated upon.

\* These analyses of treatment include only Detroit hospital cases. As stated above (page 1), it was difficult, in cases collected in this manner, to be sure that all charts were included. A careful recheck showed that very few records of patients who had had resections were omitted. Several colostomies, ileostomies and exploratory laparotomies, where the final diagnosis was not definitely established (no X-ray, operative note not positive, etc.), purposely were not studied. The tables in this section, therefore, are meant to illustrate only the observations made, and are not an exact record of the total number of cases treated or observed during the time period covered by this study.

# CARCINOMA OF RECTUM AND COLON

The chief practical importance lies in those cases where resection was attempted—where treatment offered a chance of cure. Table VIII contrasts certain data in the resected cases who recovered and in those who died after operation.

TABLE VII  
*Treatment of 222 Cases of Rectum and Colon Studied*

|                                 | Resection     |       | Colostomy;<br>cæcostomy;<br>enterostomy |       | Ileostomy;<br>sigmoidostomy |       | Exploratory<br>laparotomy |       | No<br>treat-<br>ment | Total |
|---------------------------------|---------------|-------|---|-------|-----------------------------|-------|---------------------------|-------|----------------------|-------|
|                                 | Recov-<br>ery | Death | Recov-<br>ery                           | Death | Recov-<br>ery               | Death | Recov-<br>ery             | Death |                      |       |
| Rectum.....                     | 16            | 14    | 9                                       | 5     |                             |       |                           |       | 23                   | 67    |
| Rectosigmoid...                 | 4             | 5     | 7                                       | 4     |                             |       |                           |       | 5                    | 25    |
| Sigmoid.....                    | 6             | 16    | 0                                       | 11    |                             | 2     |                           | 2     | 5                    | 42    |
| Descending colon                | 11            | 7     | 2                                       | 3     |                             | 3     | 1                         | 1     | 5                    | 33    |
| Splenic flexure..               |               |       |   |       |                             |       |                           |       |                      |       |
| Transverse colon                |               |       |   |       |                             |       |                           |       |                      |       |
| Hepatic flexure..               | 11            | 7     | 1                                       | 2     | 1                           | 1     | 2                         | 2     | 3                    | 30    |
| Cæcum and as-<br>cending colon. |               |       |   |       |                             |       |                           |       |                      |       |
| Colon unclassi-<br>fied.....    |               |       |   |       |                             | 1     | 1                         |       |                      | 2     |
| Appendix.....                   |               |       |   |       |                             |       | 4                         |       |                      | 4     |
| Diagnosis<br>not definite...    |               |       |   |       |                             |       | 8                         |       | 11                   | 19    |
| Totals.....                     | 48            | 49    | 19                                      | 25    | 1                           | 7     | 21                        |       | 52                   | 222   |

*Rectum.*—These cases are characterized by the fact that there is little obstruction present, and that a large number—almost one-third—are so far advanced when diagnosed that they are refused operation. The cases where death followed resection had had symptoms two months longer than those who recovered from resection; yet even of those who recovered, eleven of sixteen—almost three-fourths—had an operative note that the growth was already fixed, or had extended to contiguous tissues, or had metastasized. Many of those who recovered from resection died within a few months. Evidently operation must be done sooner than six months after the onset of symptoms to be satisfactory in many cases.

Concerning methods, except for the high mortality following the combined one-stage abdomino-perineal resections, the table shows nothing remarkable as regards type of operation, preliminary colostomy, *etc.* The colostomies did not seem to be done for acute obstructions so frequently as in growths higher up, but more generally as a first exploratory stage, with contemplated radical removal later.

*Colon.*—Apparently most of these cases are operated upon sooner or later—probably because so many end finally in obstruction or severe attacks of abdominal cramps. The mortality from resections is high. In general,

the cases who died following resection do not show longer duration of symptoms, more obstruction, or fewer preliminary decompressive colostomies than those who survived. Also, the operative notes concerning fixation, extension and metastasis are no more frequent in the deaths than the recoveries. The numbers are probably too few, the auspices too scattered for accurate analyses.

*Rectosigmoid.*—These growths have a long period of pre-operative symptoms—eighteen to twenty months—three times as long as rectal cancers—before diagnosis or operation. Much more relief is obtained by colostomy here than by colostomy for sigmoid growths a short distance higher, and it is done with much lower mortality.

*Sigmoid.*—In this series the mortality from resections is quite high. Where only colostomy was done, the mortality was 100 per cent. (eleven colostomies, eleven deaths). Most of these cases had marked obstruction. On the subject of colostomy in these cases Dixon\* has recently expressed himself as follows: "I believe that in cases of carcinoma of the sigmoid and rectosigmoid enterostomy is usually unnecessary. If frequent enemas and hot abdominal stupes are used the carcinoma will usually relax sufficiently to allow the contents of the intestine to pass through." Probably many of these cases were in greater extremis than patients who might be able to travel before being operated upon; yet a perusal of the charts leaves the impression that pre-operative cleansing over a period of several days is not so thoroughly carried out as Dixon, Rankin and others recommend. The operative notes in these cases, also descending and transverse colon, left the impression that the growths are not extensive—certainly not when compared to rectal cancers of the same duration of symptoms—and if removal could be accomplished satisfactorily, a favorable prognosis might be given.

*Splenic Flexure.*—All of these cases died—either following résection, colostomy or exploration. Cancers of the splenic flexure are noted for their high mortality, to which their inaccessible position contributes, and for their insidious onset, frequently being very difficult to recognize. Though some authors state that all have obstruction, some cases go on to perforation with symptoms only of left costal pain, left subphrenic abscess. In one case in this series an unsuspected abscess contiguous with the growth in the left subphrenic region was entered at the time of operation.

*Cæcum, Ascending Colon.*—Most of the hepatic and cæcal tumors were already large masses by the time they came to operation. The technical difficulties of extensive resections of the right half of the bowel are apparent. The experience here with short circuiting operations—ileo-sigmoidostomy, etc., was not good. Rankin has also noted that this operation short circuits the water absorbing portion of the bowel, and the ensuing diarrhœa contributes to the dehydration and post-operative toxæmia. He has recommended preliminary ileostomy several weeks in advance, so that the water loss can become adjusted.

*Cause of Post-operative Death.*—An analysis of post-operative causes of

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\* Dixon, C. F.: Proceedings Staff Meetings Mayo Clinic, vol. v, p. 107, April 16, 1930.

# CARCINOMA OF RECTUM AND COLON

TABLE IX

*Cause of Death Following Resection and Colostomy for Cancer of Rectum and Colon*

|                        | P.O.<br>deaths |                                      | Peri-<br>tonitis | Prob-<br>ably<br>peri-<br>tonitis.<br>Ob-<br>struc-<br>tion | Myo-<br>cardial<br>failure,<br>shock | Pul-<br>monary<br>embo-<br>lism | No<br>note | Sudden<br>hæmor-<br>rhage | Chronic<br>ne-<br>phritis |
|------------------------|----------------|--------------------------------------|------------------|---|--------------------------------------|---------------------------------|------------|---------------------------|---------------------------|
| Resections             | 13             | Rectum . . . . .                     |                  | 1   | 2                                    |                                 | 8          |                           | 2                         |
|                        | 4              | Rectosigmoid . . . . .               | 1                | 2   |                                      |                                 | 1          |                           |                           |
|                        | 17             | Sigmoid . . . . .                    | 6                | 6   | 1                                    | 1                               | 1          | 1                         | 1                         |
|                        | 7              | Descending<br>splenic trans. . . . . | 2                | 2   | 1                                    | 1                               | 1          |                           |                           |
|                        | 8              | Hepatic ascending<br>cæcum . . . . . | 1                | 3   | 1                                    | 2                               | 1          |                           |                           |
|                        | 49             | Total . . . . .                      | 10               | 14  | 5                                    | 4                               | 12         | 1                         | 3                         |
| Colostomy<br>Ileostomy | 5              | Rectum . . . . .                     |                  |   |                                      |                                 | 5          |                           |                           |
|                        | 4              | Rectosigmoid . . . . .               |                  | 2   |                                      |                                 | 2          |                           |                           |
|                        | 11             | Sigmoid . . . . .                    | 2                | 5   | 1                                    |                                 | 1          | 1                         | 1                         |
|                        | 1              | Descending<br>splenic trans. . . . . |                  |   |                                      |                                 | 1          |                           |                           |
|                        | 2              | Hepatic ascending<br>cæcum . . . . . |                  |   |                                      |                                 | 2          |                           |                           |
|                        | 23             | Total . . . . .                      | 2                | 7   | 1                                    | 0                               | 11         | 1                         | 1                         |

death was attempted. In some cases an autopsy or post-operative wound inspection gave an accurate report. Frequently, however, only a rough clinical appraisal was possible, based upon the post-operative notes, nurses' record, etc. For example, a patient dying four, five or six days after operation exhibiting continuous abdominal pain, vomiting, distention, high evening temperature, and no respiratory signs was thought to have died of peritonitis. Twelve of seventy-two deaths following resection or colostomy were due definitely to peritonitis. Using the above clinical estimate, another twenty-one were thought to have died of peritonitis or bowel obstruction, making thirty-three of seventy-two deaths due to peritonitis, probable peritonitis or obstruction. Myocardial failure, shock, were thought to be responsible for six fatalities. Pulmonary embolism, chronic nephritis (or delayed exhaustion), four each, sudden hæmorrhage, two. No data were available in twenty-three cases.

The problem in treatment, therefore, resolves itself to a great extent into the problem of preventing peritonitis. Rankin† has elaborated upon this. The organisms in the colon are virulent, and are easily squeezed into adjacent tissues by operative handling, especially mobilization of an adherent growth. In addition to leakage from failure of coaptation, there may be necrosis due to inadequate blood supply, or post-operative distention may cause strain on the suture line. Pre-operatively reducing the local infection to a minimum by high caloric, scant residue diet for several days, and overcoming the anæmia and dehydration are most important. Pre-operative heightening of the body immunity with colon vaccine, aseptic resections, absolute post-operative bowel rest are aids.



## THE PATHOLOGY ASSOCIATED WITH RUPTURE OF THE SUPRASPINATUS TENDON

BY ERNEST A. CODMAN, M.D. AND IRVING B. AKERSON, M.D.  
OF BOSTON, MASS.

IT MAY seem out of place in discussing the above subject to give a brief history of the Registry of Bone Sarcoma, but since it is due to the existence of that Registry that this article is written by a surgeon in this special number of the ANNALS OF SURGERY, I feel that a few words of explanation are necessary. I am not a pathologist and have very little more claim than any other surgeon who learned his pathology in 1894 to entitle me to have an article in this number. My excuse in this instance is my association with Doctor Ewing on the Committee of the Registry of Bone Sarcoma. My interest in the pathology of bone tumors was aroused in 1920 by a case which came under my care. This patient was the wife of one of my best friends, a man of keen intelligence with a splendid regard for the plain truth. I told him how little there was known about bone tumors and how difficult it was to find any exact facts about cases which were claimed to have been cured. He offered to pay the expenses if I would undertake to write to all my surgical friends and find out if there actually were any cured cases of bone sarcoma. Before I had been able to run down many cases which had survived any kind of treatment long enough to be considered cures, my patient died. An autopsy revealed that the tumor was metastatic carcinoma and was not a primary sarcoma of bone.

Even after a pathologic specimen was obtained at autopsy there was still doubt of the diagnosis and in fact there still is, for no primary tumor was found at autopsy and the origin of the metastasis remains unsolved. These facts and those gleaned from my correspondence, demonstrated to me very clearly that the entire knowledge of the diagnosis and treatment of bone tumors was very obscure and of very little practical consequence to an individual patient. Meantime I had amassed so much correspondence concerning alleged cures from many of the most prominent surgeons and pathologists in the country, that it seemed a pity to give up the investigation even though it could never be of use to my patient. The result was the formation of the Registry of Bone Sarcoma which was financed by the American College of Surgeons.

The writer was appointed registrar with Dr. Joseph C. Bloodgood and Dr. James Ewing as the other members of the committee. At that time I was also inspired by the hope of making this one disease an example of what I had previously called the End-result System of Hospital Organization, in which for the previous decade I had been intensely interested as a member of the Committee on Hospital Standardization. I was willing to

give up more than half my time to the Registry with the hope that in this one disease I could get all the hospitals in the country to record (*i.e.* register) whatever instances came within their doors. All I asked was a brief, truthful record of each case, with X-ray films and pathologic slides, and if the patient were treated, an annual notation of his condition. The data thus collected would be studied by our committee with a view to obtaining more satisfactory methods of diagnosis and treatment, and data were to be submitted to as many other pathologists as we could induce to study them. My interest in the success of the Registry was wholly in showing that it was possible (as a matter of human nature) for the surgical profession of this country to get together in giving a truthful account of what happened to patients afflicted with this one rare disease, even though the record of each case should be a record of error in diagnosis and treatment. If we could be sure that every hospital in the country was giving proper diagnostic facilities, proper X-ray technic and interpretation, proper pathological skill and knowledge, and judicious and skillful surgical treatment to cases with this one disease, we would at the same time be showing that they were capable of (and probably giving) a similar grade of service to other patients with other diseases. The ability to register a case was not only a criterion of the equipment and skill of a hospital staff, but also a criterion of its ability to coöperate and of its organization, because unless the organization of a hospital was of a high grade, sufficient pressure could not be used on any individual in a staff who had failed to diagnose or treat rationally one of these cases, so that he would permit publicity of the facts with a truthful account of his errors. Since errors in diagnosis and of judgment in treatment were the rule in cases of this lesion, no harm would be done.

From my point of view, the Registry of Bone Sarcoma has been a miserable failure. I was disappointed in the ability and zeal of the staffs of even the Class A hospitals to register their cases truthfully. Two of the greatest private institutions in this country would not coöperate. Naturally, with this illustrious example, many of the other hospitals shirked or failed to take the trouble to register their cases. However, a large number of hospitals (particularly those which were untrammelled by academic affiliations, by traditions of antipublicity or by consciousness of being business enterprises), registered their cases, so that in spite of the failure of the real purpose of the Registry, a considerable amount of data was accumulated for scientific study by the committee and interest in the study of bone tumors was generally aroused. That this material was used by Dr. James Ewing to complement and augment his already great knowledge and experience in this subject, saved the Registry from utter failure.

Everything that the Registry has really accomplished is due largely to the brain of Doctor Ewing. It was his guidance that led to the classification of bone tumors, which though admittedly imperfect, is now the accepted classification. Dissemination of knowledge about the form of round-cell sarcoma which has come to be called Ewing's sarcoma was accomplished very largely

by the Registry, but the separation of this tumor from the other bone sarcomas was made by Ewing even before the Registry had made any publication whatever. So while the Registry has helped, it was Ewing who brought the attention of the profession to the fact that this form of tumor is clinically an entity. The almost voluminous literature which has accumulated in consequence of the interest aroused by the Registry has been dominated for a decade by Doctor Ewing's thought. Kolodny's book, which is, at present, by far the most accurate presentation of our knowledge of malignant bone tumors, is admittedly an expression of Ewing's ideas. I feel that the best that can be said for the Registry is that it has helped to crystallize and diffuse the knowledge of bone pathology which James Ewing had accumulated during his previous years of study.

During my five years as registrar, I was in constant touch with Doctor Ewing. He painstakingly reviewed nearly every case which was registered, wrote his opinion at the time, and, in perhaps half the instances, reviewed the case a second time a year or more later to see if his opinion had been modified. He was a constant source of inspiration and encouragement to me as I labored over the detailed work, for I felt that my time was well recompensed in having the material which I had collected studied by him. In spite of his great knowledge and experience, some of his earlier diagnoses had to be corrected later, and I found him always ready to discuss all points made by other pathologists, and to give them due weight. He could modify his own opinion if the comments of the other pathologists enlightened it at all. I spent many hours with him discussing the cases and although he knew how limited my knowledge of pathology and histology was, he was always ready to listen to my opinion and suggestions. If he disagreed, he frankly said so. If I was able to show him something he had overlooked, he was quite ready to accept it. His frankness and patience in these long discussions were remarkable, for I know that I was taking his time from other valuable work. My duties as registrar brought me into intimate contact with many other pathologists and I learned that so far as bone tumors were concerned, no pathologist, even Ewing himself, had accurate knowledge. It was a subject on which "a cat might look at a king." My intensive study of these cases gave me an advantage, although I knew little of pathology in general, and I was able to see that so far as the histologic diagnosis of bone tumors was concerned, a surgeon who could interpret X-ray films and who knew the clinical story of the cases could make the diagnosis as accurately in most cases as the pathologist could with the average inadequate material which is given to him by surgeons from specimens taken at exploration. If the combined clinical and röntgenologic opinion was in doubt, it generally proved that the pathologist was in doubt from the section.

I perhaps grew overconfident in my remarks to pathologists, contending that the X-ray film was in a measure as important a method of determining pathologic conditions as was a microscopic section. The X-ray film is not as a rule understood by pathologists. They do not realize that it is an accurate

chart of the relative atomic weights of all substances encountered by the rays on the way to the plate beneath the object shown. After all, a microscopic section is only an extremely thin slice of a part of the whole object. It varies with the direction in which the slice is taken, with the part that it is taken from, and with the artificial staining of the materials used to make it visible under the microscope. It is thus subject to much inaccuracy. From my point of view, the pathologist who neglects to study the X-ray film of a bone tumor is in much the same position as a röntgenologist who undertakes to contradict an opinion made from the microscopic slide. The film shows the manner in which the bone is eroded by the disease or enhanced by deposit of calcium. In a way it shows more than does a median section of the gross specimen.

I had been lecturing Doctor Ewing on this favorite theme (on which by the way he agreed) when the conversation turned to living pathology *versus* autopsy pathology. I argued that we surgeons saw many evidences of pathology in the living which the laboratory pathologist never saw. I instanced rupture of the supraspinatus tendon and Doctor Ewing admitted that he had never heard of it. I think the majority of other pathologists will admit the same. The subject of this paper is now introduced.

At the ordinary autopsy there is much to be done and much to be recorded and it is unusual for the joints to be opened and observations on their pathology added to those referring to the viscera. Still more unusual is it to open the bursæ. Consequently, few pathologists ever open the subacromial bursa to study its pathology. This has been my hobby for thirty years. Whenever possible when attending an autopsy, I would ask for permission to open the subacromial bursa. I have also opened the bursa in many cases in the dissecting room at the Harvard Medical School, and I have had the opportunity to open it more than a hundred times in the living. In consequence of this experience, I have found that in elderly subjects (particularly in working people), the incidence of ruptured supraspinatus tendon is large. Unfortunately, I have not kept accurate account of the numbers of my observations, but I have always been able to find at least one instance of one of these ruptures in every set of twenty dissecting room subjects. I therefore formerly felt that the incidence in this class of material was surely over 5 per cent., but this work of Doctor Akerson's\* has opened even my eyes.

The present study has been made from autopsy material obtained at a large municipal hospital (Long Island Hospital) for chronic conditions. The patients sent to this hospital are people who are aged and down-and-out, and owing to the chronic character of their diseases, cannot be cared for at the other Boston hospitals. Doctor Akerson has made a study from 100 specimens taken from fifty-two consecutive autopsies and the percentage of

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cases showing evidence that the supraspinatus tendon had been ruptured at some time during the lives of these patients is high—39 per cent. It may, therefore, be taken as a maximum and it may be expected that pathologists performing routine autopsies in general hospitals for acute diseases, where the ages average considerably younger, will find a decidedly smaller percentage. We have made no attempt to correlate the past histories of these patients as to trauma or occupation with the autopsy findings. It would have been hardly possible under the circumstances.

As a routine method of examination of these cases, we recommend the pathologist to employ the form of incision which we use in operations on the living. A cut is made on the anterior aspect of the shoulder-joint from the acromioclavicular articulation downward for about two inches. The fibres of the deltoid are separated and retracted and the roof of the bursa is incised between two pairs of forceps as one opens the peritonæum. When the lips of the wound are retracted, the whole inferior aspect of the bursa can be made to pass in review by rotating the humerus. The base of the normal bursa is smooth and spherical and almost as colorless as the cartilaginous surface of the head of the bone, though it lacks the bluish lustre of cartilage. Most rents in the tendons of the short rotators usually appear in this base as communications directly into the joint and are readily visible. Occasionally the tendon is ruptured beneath the base of the bursa, which is left intact. In the ordinary autopsy it would take but a few minutes' extra time to examine both bursæ. If lesions are found, the head of the bone with the insertions of the short rotators can be removed and studied. This was the method used by Doctor Akerson and his findings are good evidence that some sort of pathological process has been at work in the subacromial bursæ of these patients during their lifetime. One must understand that these findings are those accumulated by each individual subject in many years. They are end-results, not acute lesions. In asking Doctor Akerson to make this study, I have told him how important it is for surgeons to find out whether these lesions are usually of a traumatic nature, or whether a diseased or weakened condition of the tendon precedes the trauma and the rupture actually occurs through pathologic tissue.

There are four reasonable hypotheses to explain these lesions: (1) They may be the results of trauma (*i.e.*, rupture of tendon fibres, followed by imperfect repair). (2) The defects left as a result of the so-called "calcified deposits." (3) The result of necrosis of the tendon or other diffuse, pathologic process, or of the same phenomena which are known as arthritis in other joints. (4) The direct result of attrition (hypothesis of Meyer).

From the clinical and especially from the industrial point of view, it is very important that these questions should be answered. On the one hand, thousands of dollars paid annually by insurance companies, and, on the other hand, the question of utter poverty of many individuals, may depend upon this answer. My own experience has led me to the conviction that rupture of the supraspinatus tendon is by far the most common cause of industrial

## RUPTURE OF THE SUPRASPINATUS TENDON

shoulder disability and that complete rupture is a more painful, more serious, and more disabling lesion than fracture of the humerus or dislocation of the shoulder. It is the usual cause of traumatic subacromial (subdeltoid) bursitis. I am at present writing a book to support this contention. Since I have been able clinically to diagnose cases of supraspinatus rupture with only a small percentage of error, and have in more than 40 cases sutured the ruptured tendon, my own conviction is naturally in favor of a traumatic cause. Yet I am by no means convinced that there is not an underlying degenerative process in the tendon which makes it prone to rupture. The frequency of finding that this is a bilateral condition, together with the fact that the lesion seldom occurs in young men, makes it highly probable that there is some general cause, which, with the trauma, produces the condition which we are studying.

I may not be correct in my contentions, but there is no doubt that Doctor Akerson has found defects in the supraspinatus tendon which might be explained as the results of traumatic rupture in thirty-nine out of 100 shoulder-joints taken from aged people of the laboring classes.

The object of this paper is to bring the attention of pathologists to a lesion which is of great importance in industrial surgery and which in the opinion of the writers, needs intensive study.

### *Doctor Akerson's Findings in 100 Shoulder Joints*

|   |         |               |
|---|---------|---------------|
| Both shoulders examined.....                        | 48      |               |
| Single right shoulders.....                         | 2       |               |
| Single left shoulders.....                          | 2       |               |
|   |         | 100           |
| Total autopsies .....                               | 52      |               |
| Males, 37; females, 15; total.....                  | 52      |               |
| Ages: 46-59 .....                                   | 7 cases | } Total ..... |
| 60-79 .....   | 35 "    |               |
| 80 and over .....                                   | 10 "    |               |
| Right shoulders, 50; left shoulders, 50; total..... | 100     |               |

### *Rupture of Supraspinatus Found*

Right, 23 (46 per cent.); Left, 16 (32 per cent.); Average, 39 per cent.

### *Degree of Ruptures*

|  |    |
|--|----|
| Large enough to show the articular surface on opening bursa..... | 21 |
| Smaller than this but still quite apparent.....                  | 18 |
| Total .....  | 39 |

In thirty-nine cases the supraspinatus was ruptured either alone or in combination with adjoining tendons as follows:

|  |    |
|--|----|
| With portion of subscapularis.....                   | 6  |
| With portion of infraspinatus.....                   | 10 |
| With infraspinatus and teres minor.....              | 2  |
| With all other short rotators (in same patient)..... | 2  |

In only one case was a lesion found in other tendons (a small lesion in the infraspinatus) when the supraspinatus was intact.

The joint cartilage showed erosion in twenty-four cases in which the supraspinatus had been torn. No erosion was shown in any case in which the supraspinatus was not torn or when the tear was so small as not to expose the bone or cartilage when the bursa was opened. The amount of erosion was usually proportionate to the extent of damage in the tendon.

*Condition of Biceps Tendon in 50 Cases*

|                               |    |
|-------------------------------|----|
| Exposed to view in gap.....   | 1  |
| Could be pulled into gap..... | 2  |
| Evulsed from glenoid.....     | 6  |
| Flattened .....               | 4  |
| Frayed .....                  | 5  |
| Total .....                   | 18 |

Bearing in mind that this series of lesions must represent the scars or attempts at repair of trauma or disease which had probably occurred many

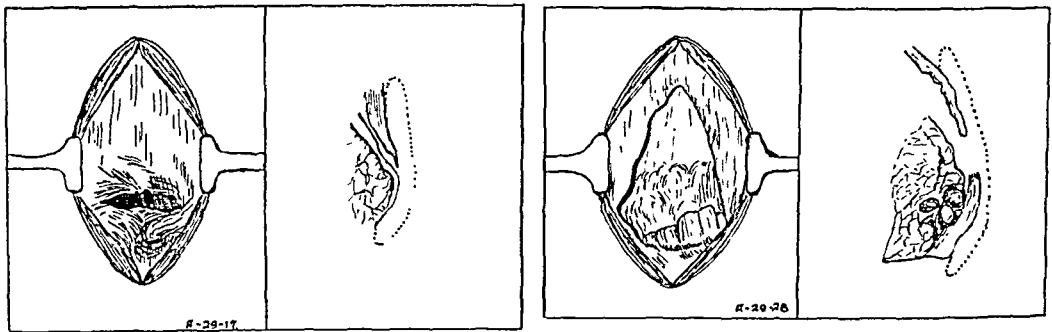


FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 1.—A transverse tear of the tendon. At the base of the defect (shaded portion), is articular cartilage.

FIG. 2.—Vertical section near edge of same specimen as in Fig. 1. A falciform edge on the ruptured tendon and a rounding off of the tuberosity.

FIG. 3.—Here we see a triangular tear in the tendon. There are stubs of tendon on the tuberosity in a characteristic palisade-like formation.

FIG. 4.—A tag of tendon on the tuberosity. The tendon is retracted and thinner than the stub. In the tuberosity are small cyst-like cavities.

years previously, it seems fairly obvious that these defects in the tendon rarely, if ever, undergo complete repair. One may be reasonably sure from the series of lesions observed, as well as from findings at operations on the living within a few weeks or months after an injury, that the sequence of events is somewhat as follows:

1. A transverse rupture occurs across the breadth of the tendon near its insertion (Fig. 1).

2. Retraction of the muscle causes the rent to assume a triangular shape with its base on the tuberosity (Fig. 3).

3. A feeble effort at repair takes place, resulting in (a) rounding of the triangle by obliteration of the corners (in the horizontal plane) and (b) the formation of a falciform edge (in the vertical plane) of fibro-synovial tissue

## RUPTURE OF THE SUPRASPINATUS TENDON

which smooths the edge of the rupture around the whole circumference (Figs. 5 and 8).

4. Gradual absorption of the tag of tendon which remains on the tuberosity (Figs. 7 and 8).

5. Recession of the now useless portion of the tuberosity to which the tendon was formerly attached (Fig. 8).

6. The formation of fibrocartilage on this surface to avoid friction as the tuberosity passes in and out under the acromion (Fig. 8).

Thus we may feel moderately sure that nature's method of repair is a palliative smoothing off of the rough edges rather than a restitution of substance. This must be true whether the cause of the defect is purely traumatic or the result of absorption from disease. This whole process takes many months or even years.

I have referred above to the question of interpretation of the findings in this series. There is little doubt that in a similar series of autopsies, the lesions above described will be found by any pathologist who cares to look

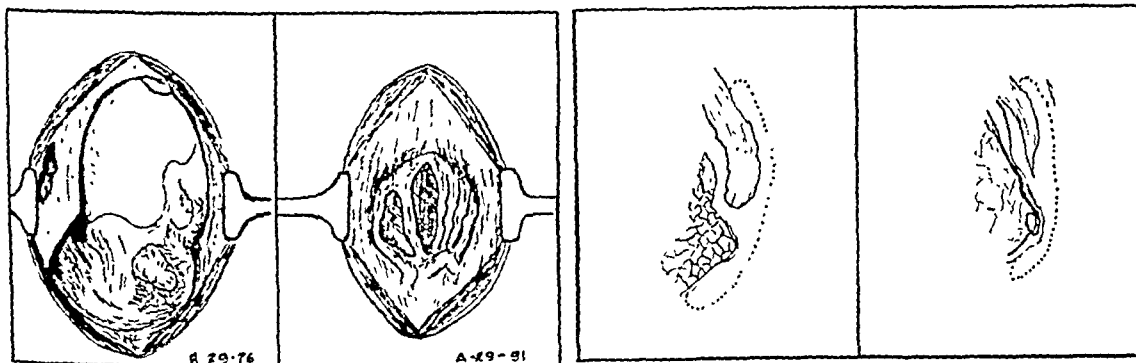


FIG. 5.

FIG. 6.

FIG. 7.

FIG. 8.

FIG. 5.—Extensive rupture involving supra- and infraspinatus. There is a smaller tear to the left. The wavy line represents the edge of the articular cartilage. There is new bone on the bare tuberosity.

FIG. 6.—Bands of tendon still crossing the defect. At the right are several slits in the tendon, i.e., the superficial laminae have torn away, but bands of the deeper portion of the tendon remain.

FIG. 7.—The tuberosity is receding and the edge of the tendon is rounded and blunt as compared to that in Fig. 8, which is more common and is falciform.

FIG. 8.—Shows a further rounding off of the tuberosity as compared to Fig. 7. Cartilage is forming over the exposed tuberosity.

for them. How will such lesions be interpreted in the future when they have been studied from the clinical and operative side as well as from the pathologic findings? We can touch briefly on some of the problems which have occurred to us.

*In Favor of the Traumatic Origin.*—(1) Foremost is the fact that there exists a clinical symptom-complex by which rupture of the supraspinatus can be diagnosed. The patient has a history of a considerable trauma; he can raise his arm only with great effort, if at all; there is lack of normal scapulo-humeral rhythm; there is a tender point corresponding to the facet of insertion of the supraspinatus where a slight sulcus and a slight eminence can be felt; there is a painful jog and characteristic crepitus as this tender point disappears beneath the acromion as the arm is elevated.

(2) The findings at operation are similar to those lesions which have



been found in this series at autopsy, although in the main those found at operation represent earlier stages of repair.

(3) Microscopic sections from cases in this series indicate loss of continuity of the fibres without serious signs of disease in the adjacent tendon.

(4) The supraspinatus tendon (perhaps owing to man's vertical position), is the locus minoris resistentii and is almost always involved. The rents in the other tendons extend laterally from that in the supraspinatus, even to the extent of evulsion of all of the tendons of the short rotators.

(5) The preponderance of right over left speaks for trauma.

*Against a Traumatic Origin.*—(1) Tissue removed from tendons of aged people and from cases operated on for lesions in this region, whether traumatic or not, show a necrosis which is a result of retrograde changes. This necrosis is similar in appearance in cases operated on for calcareous deposits. It is so common as to suggest it is a semi-normal senile change.

(2) The large number of bilateral cases (fourteen) found at autopsy, speaks against traumatism and in favor of some form of slow necrotic destruction.

(3) The general surgical profession has not recognized this lesion as a clinical entity which can be diagnosed and repaired by operation as claimed by Doctor Codman.

*In Favor of These Lesions Being the Results of Calcified Deposits.*—Since the X-ray was introduced, calcified deposits have been found many times in the supraspinatus tendon and in some of the other neighboring tendons. It is not uncommon for these deposits to be removed by surgery, but experience shows that all such deposits are absorbed sooner or later, even if not removed. That the lesions found in our series might in many cases be merely the defects left by previous calcified deposits must be admitted. Calcified deposits are often bilateral; so are these defects in the supraspinatus.

The exact method of formation of these deposits is not known. Sections from them indicate that where they exist, there is loss of continuity of the fibres of the tendon. It seems doubtful if, when they are absorbed, new tendon ever forms. It cannot be denied that the findings above described may in some cases be the defects left by these lesions, or we may assume that tendons weakened by such lesions in the past may tear readily.

*In Favor of These Lesions Being the Result of Necrosis of Constitutional Origin.*—This heading is inevitably associated with the question of arthritis. It includes it perhaps. The shoulder-joint (owing to its freedom in all directions, without close relations with other bones) is anatomically not likely to show the usual changes associated with arthritis. The joint is really made up of the short rotators, which, near their insertions, are blended with the capsule. Should we not expect therefore, that the arthritic changes common in other joints might appear in the shoulder-joint in the form of defects in the supraspinatus and other short rotators? One might open a subacromial bursa, see a defect in the supraspinatus with the asso-

ciated atrophic and hypertrophic changes on the tuberosity and be satisfied with the diagnosis of arthritis. Space does not permit us here to enter into an extensive argument on the matter. Suffice it to say that we do not consider the changes found as comparable to such changes as are called arthritis in the hinge joints.

*In Favor of the Theory That These Changes Might Be Caused by Friction.*—We must refer to the writings of Dr. A. W. Meyer, Professor of Anatomy, Leland Stanford University, California. Doctor Meyer made an excellent case for the argument that laboring men using their shoulders to excess may actually, by friction between the humerus and the acromion, wear through the supraspinatus tendon and joint capsule, and even destroy the biceps tendon as it courses across the joint over the cartilaginous head of the bone.

From our understanding of accepted principles of pathology, such actual destruction by friction is well nigh impossible, but we grant that the same results may be brought about by persistent inflammation of these structures, caused by friction. Chronic inflammation in any structure tends to produce an initial hypertrophy followed by atrophy. We feel that it is conceivably possible that defects similar to those found in this investigation might come about from excessive overuse without a single serious trauma. We feel that such a consequence is unlikely and that in view of our clinical experience in which these lesions have been found within a few months after adequate injuries, the burden of proof is on those who feel that chronic overuse might produce extensive defects in the tendons inserted into the head of the humerus.

A purely anatomic argument against Doctor Meyer's theory is that the impingement of the head of the humerus on the lower surface of the acromion does not occur in the normal individual. The friction at this point is taken up by the outer side of the tuberosity which is covered with the lower surface of the bursa. Furthermore, the coraco-acromial ligament partially intervenes. The plane of the cartilaginous surface is distinctly below the plane of the tuberosity as the arm is abducted. As soon as the tendon is damaged, however, either by disease or trauma, there would be a marked jog in the motion at just the point at which the uppermost fibres of the normal tendon are inserted into the tuberosity. A trauma affecting these fibres would therefore start a vicious circle, changing the contour of the lower surface of the bursa so that there would always be a hitch at the point where this portion of the base passed beneath the acromion and coraco-acromial ligament. Chronic inflammatory changes would take place.

One is tempted to compromise by saying that many causes or combinations of causes may produce the same lesion; *i.e.*, a defect in the substance of the supraspinatus tendon.

*e.g.*: Constitutional conditions might produce changes similar to those produced in atheroma of the arteries. A trauma ordinarily easily withstood might rupture such a tendon.

*e.g.*: A calcified deposit absorbed some years before might have destroyed enough tendon fibres so that a slight trauma later might rupture the remainder.

*e.g.*: A young man might rupture fibres which his active blood-supply would completely repair; one slightly older might fail in repair and have a calcified deposit form in a poor cicatrix; an elderly man might fail to repair such a rupture altogether, and show at autopsy the condition we find.

*e.g.*: Continued overuse might cause necrosis and atrophy. Laminated band after laminated band might break away from slight strains. A single severe trauma might complete the havoc.

Neither of us at present cares to take a very positive stand in explaining these findings. We are inclined to think that changes in the integrity of the tendon due to age, constitutional conditions or overuse are primary as a rule, but that trauma produces the actual rupture in most instances. The fact that these cases can be diagnosed clinically and the rupture sutured, influences our interpretation of the autopsy findings.

It is sometimes well to make comparisons. Consider the relative amount of pain and disability caused by bone sarcoma and by injuries to the supraspinatus. Unlike bone sarcoma, which is never diagnosed in an early stage and is seldom cured, rupture of the supraspinatus can be recognized early and promptly sutured. Contrast the literature of the two lesions. It would take hundreds of volumes to bind the literature of bone sarcoma, a dramatic, pathetic, rare condition, for which we can do next to nothing and which is of little industrial importance. On the other hand, the literature on rupture of the supraspinatus tendon, the most common cause of prolonged shoulder disability in industry, and a subject of great importance, has only just begun!

It seems as if hitherto pathologists had interested themselves only in diseases which may cause death. Modern industry now urges the pathologist to search for the causes of incapacity.

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\*So far as I know there is at present no literature on the subject of this paper which deserves serious study, except that comprised in the above references. I have no doubt that Doctor Meyer and I refer to the same lesions which were studied by Doctor Akerson for this paper and can be found by anyone who wishes to look for them in similar material. Doctor Meyer's attention has been focused on the long head of the biceps; mine has been focused on the supraspinatus. Probably both of us are in a measure right, and in great measure wrong, but at least we have opened up the field for future students who wish to relieve persons incapacitated by lesions in this region of the body.

# L'ÉPITHÉLIOMA ÉPIDERMOÏDE DU COL DE L'UTÉRUS A KÉRATINISATION PÉRILOBULAIRE

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LA VARIÉTÉ d'épithélioma sur laquelle nous attirons l'attention est caractérisée essentiellement par une anomalie histologique: les cellules, dont sont formés les cordons et les lobules du tissu néoplasique, au lieu d'évoluer et de se transformer en squames kératinisées de la périphérie au centre de ces cordons et lobules, comme on le constate habituellement, évoluent et se transforment du centre à la périphérie (ou bien simultanément dans les deux sens), de sorte que les cellules génératrices sont intérieures, au lieu d'être périphériques, et qu'il se forme une couche cornée au contact même du tissu conjonctif.

Cette anomalie, qui n'est pas très rare, est facile à constater. Néanmoins nous n'en avons trouvé aucune mention dans les ouvrages que nous avons consultés.

Voici la description complète, clinique, thérapeutique et histologique, d'un cas typique de cette variété.

CAS I (XIV—A, n° 614). Pl. . . ., cinquante-neuf ans.—Tumeur maligne du col utérin, degré II.

*Histologie*: épithélioma épidermoïde, kératinisation à la fois centro-lobulaire et péri-lobulaire.—Premier traitement curiethérapique, suivi d'hystérectomie. Récidive dans la cicatrice vaginale.—Deuxième traitement curiethérapique; survie actuellement de trois ans.\* Début des symptômes en décembre 1925: leucorrhée, petites hémorragies à l'occasion des rapports sexuels. Hémorragie abondante au début d'avril 1926.

1926, 20 avril.—Premier examen à la Fondation Curie. Gros col utérin, dur, ulcéré au centre, lèvre antérieure fendue; cul-de-sac vaginal gauche rétréci et induré; utérus encore mobile; par le toucher rectal, on trouve un ganglion occupant la partie moyenne du paramètre gauche.—Degré II.

## DU 22 AVRIL AU 5 MAI, PREMIER TRAITEMENT

Du 22 au 26 avril, *curiethérapie intérieure*: (a) sonde intra-utérine en caoutchouc, contenant trois tubes de radium bout-à-bout; teneur totale des tubes utérins 33,32 milligrammes de Ra-élément; filtration platine 1 millimètre; (b) dans le fond du vagin, trois tubes de radium, chacun dans un étui de liège (deux tubes maintenus par un colpostat dans les culs-de-sacs latéraux, un tube dans la concavité du ressort); teneur totale des tubes vaginaux 33,32 milligrammes de Ra-élément; filtration platine 1,5 millimètres. Dose utéro-vaginale totale 47,5 millicuries de radon détruit, par application continue, en quatre jours.

Du 27 avril au 5 mai, *curiethérapie extérieure*, limitée au côté gauche du bassin;

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\* Observation clinique et radiologique du Dr O. MONOD.

trois champs d'irradiation, ayant chacun une surface de 150 centimètres carrés : un champ iliaque antérieur, un champ sacro-iliaque postérieur, un champ ilio-fémoral transversal ; charge de radium quatre grammes ; distance dix centimètres ; filtration platine 1 millimètre. Dose 270 millicuries de radon détruit par champ en trente-quatre heures d'irradiation effective, échelonnées sur neuf jours. Ce traitement s'est effectué sans incident.

15 juin.—*Hystérectomie* abdominale totale exécutée, comme il était préalablement convenu, par le chirurgien de la patiente.

13 octobre.—Fond du vagin et paramètres indurés, sans ulcération, ni tumeur.

1927, 26 janvier.—Petite tumeur dure, d'environ 1 centimètre de diamètre, ulcérée, siègeant sur la cicatrice opératoire vaginale. *Biopsie* ; l'examen histologique indique : *récidive*.

#### DU 7 AU 12 FÉVRIER, DEUXIÈME TRAITEMENT

*Curiothérapie intérieure* : dans le fond du vagin, deux d'abord, puis trois tubes de radium (même dispositif que pour le premier traitement) ; dose 27,8 millicuries de radon détruit, par application continue, en cinq jours. Aucun incident.

6 avril.—Disparition de la lésion. Cicatrisation. Induration du tissu conjonctif pelvien, sans tumeur. Aucun symptôme fonctionnel.

14 décembre.—Bon état général. Persistance de l'induration du tissu conjonctif pelvien. On soupçonne que le néoplasme fermé continue d'évoluer lentement.

1928, 4 juillet.—Exploration. Même état.

1929, 10 avril.—Exploration. Même état.

1930, 2 avril.—Exploration. Nodosités suspectes contre la paroi pelvienne, à gauche, perceptibles par le toucher rectal.

Trois ans se sont écoulés depuis le deuxième traitement, sans qu'une récidive apparaisse avec évidence.

*Analyse Histologique du Cas I.*—Il a été fait deux analyses histologiques : l'une de la tumeur primaire (prélèvement d'avril 1926), l'autre de la récidive (prélèvement de janvier 1927). La structure est la même. Il s'agit d'un épithélioma d'origine épidermique à évolution épidermoïde.\*

Le point de départ de la tumeur paraît être dans le canal cervical ; on trouve, en effet, un peu avant le point de transition entre l'épithélium pavimenteux et l'épithélium à cellules prismatiques, des signes indiscutables de transformation cancéreuse de l'épithélium pavimenteux, qui est soudé au tissu cordonal-lobulé de l'épithélioma.

*Disposition architecturale.*—Le tissu néoplasique est constitué par des cordons épais, renflés souvent en lobules. Ces cordons ne forment pas de réseau, et leur anastomose est rare. Les renflements lobulaires présentent fréquemment des incisures périphériques, et ils sont souvent au contact de cordons plus petits, ce qui témoigne de la formation de ramifications ou de bourgeons. Toutes ces formations ont des contours arrondis et parfaitement bien limités.

Le tissu conjonctif qui sépare les cordons ou lobules forme ordinairement de larges travées.

*Structure du tissu néoplasique.*—La partie reproductrice du tissu est une couche généralement épaisse de cellules qui n'ont pas de contours nets (protoplasma indivis). Les noyaux sont arrondis ou ovoïdes, quelquefois un peu bourgeonnants et incisés à leur

\* Modifiant quelque peu la terminologie communément usitée en Amérique, et exposée par EWING (*Neoplastic Diseases*, 3<sup>e</sup> édition, 1928), nous avons pris l'habitude depuis longtemps de distinguer les épithéliomas d'origine épidermique en deux groupes : les *épidermoïdes* dont les cellules se transforment finalement en squames, et les *non-épidermoïdes* dont les cellules ne se transforment pas en squames, les uns et les autres comportant plusieurs variétés.

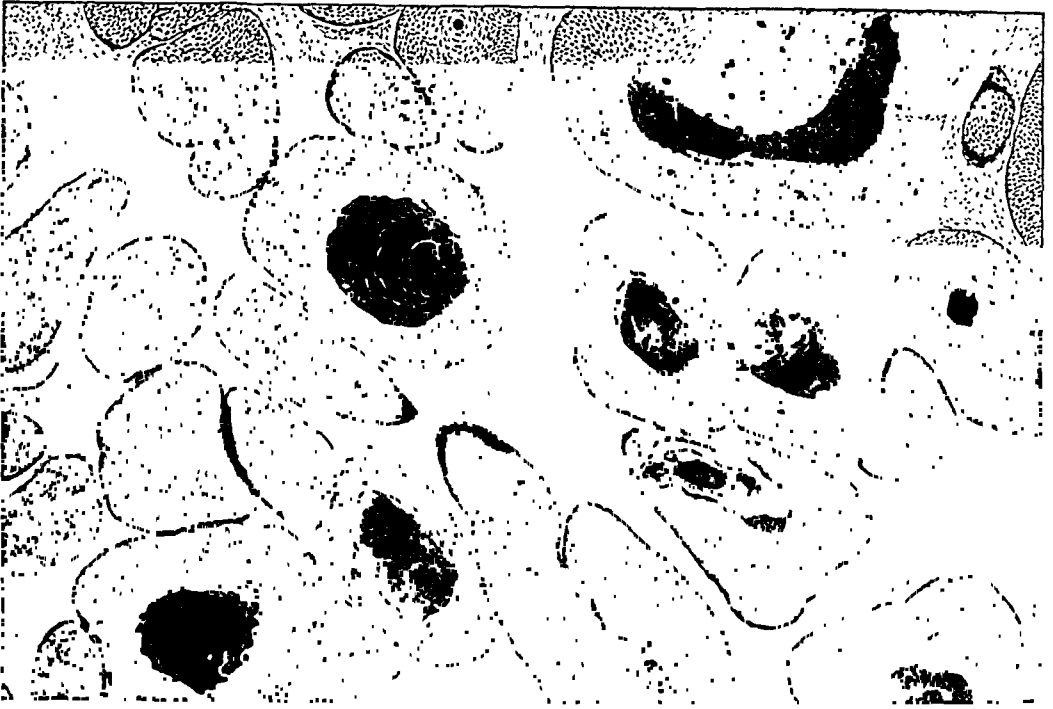


FIG. 1.—Cas Pl. . . , épithélioma épidermoïde du col de l'utérus, à kératinisation à la fois centrolobulaire et périlobulaire. Fixation par un mélange de bichlorure mercurique, formaldéhyde et acide actéique; coloration par l'hémalum et l'éosine.—Grossissement du dessin: 85.

Remarquer: l'architecture cordonale-lobulée;—le stroma conjonctif, formé de travées larges, très pauvres en cellules migratrices; dans beaucoup de lobules et cordons, un amas intérieur (central ou excentrique) de cellules kératinisées; dans quelques uns, des cellules kératinisées isolément; tous les cordons et lobules sont limités, au contact du tissu conjonctif, par une mince couche, plus fortement colorée (couche cornée périphérique). Près du bord inférieur du dessin, coupe d'un tube glandulaire.

périphérie; dans les parties les plus jeunes du tissu, ils sont serrés les uns contre les autres; leur chromatine est formée de grains et de mottes généralement denses. Dans le

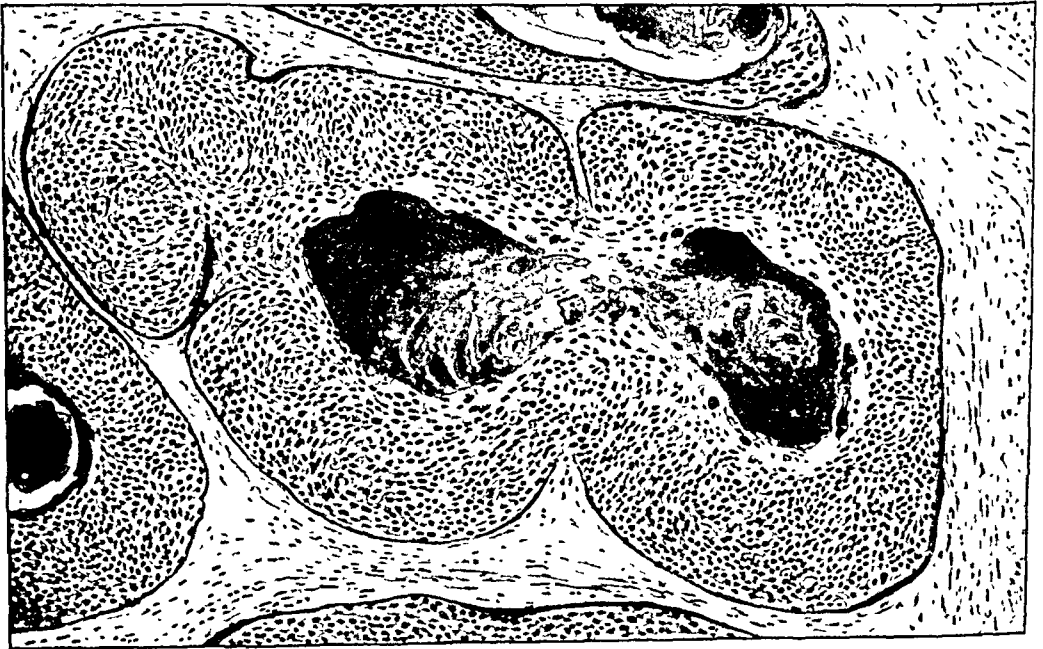


FIG. 2.—Même préparation.—Grossissement du dessin: 175. Un lobule de l'épithélioma.

protoplasma on rencontre des fibres fortement colorables par l'éosine, isolées ou fasciculées, qui ont le même aspect que les fibres d'Herxheimer d'un épiderme normal. Ce tissu ressemble à une "couche génératrice d'épiderme," qui serait anormalement épaisse.

On rencontre de nombreuses karyokinèses, disséminées dans toute l'épaisseur du tissu germinal. Les monstruosité nucléaires ne sont pas rares.

*Evolution cornée.*—Dans la partie centrale des cordons et lobules, il existe des cellules kératinisées, quelquefois isolées, le plus souvent agglomérées en amas plus ou moins volumineux. D'autre part tous les cordons ou lobules sont limités par rapport au tissu conjonctif par une couche mince et continue de cellules kératinisées. La kératinisation s'effectue donc dans deux sens opposés: en direction du centre ou mieux de l'axe des cordons, en direction de leur surface périphérique.

(a) Kératinisation centrale.—Elle n'existe que dans les plus gros cordons, renflés en lobules. L'amas axial ou central est formé de squames lamelleuses ayant conservé un noyau dense et homogène, ou de fragments de cellules sans noyau. Ces débris tantôt sont disposés sans ordre, tantôt montrent une disposition concentrique rappelant les globes cornés, tantôt semblent dissociés.

Entre le tissu actif et l'amas central kératinisé, tantôt il y a, tantôt il n'y a pas une couche de transition. La couche de transition est formée de grands corps cellulaires



FIG. 3.—Même préparation—Grossissement du dessin: 800.  
Vue partielle de deux lobules contigus; tissu germinatif formé par une épaisse couche de cellules à limites indistinctes; pas de filaments unitifs du type Schultze-Ranvier, mais en quelques points une structure fibrillaire; kératinisation périphérique aboutissant à la formation de squames plates nucléées. Au centre des lobules, amas de squames cornées agglomérées; à la périphérie, les squames forment une couche mince composée de une à trois épaisseurs de cellules.

à contours assez distincts, possédant un noyau grand et vésiculeux; autour du noyau on voit quelquefois des corpuscules rappelant les gouttelettes d'éléidine de Ranvier, et assez souvent des faisceaux de fibrilles colorables par l'éosine. La couche de transition contient des cellules qui se kératinisent isolément.

Assez souvent l'amas kératinisé est excentrique, voisin de la périphérie du lobule ou même contigu au tissu conjonctif.

(b) Kératinisation périphérique.—Elle est constante. Tous les cordons, tous les lobules, sans exception, sont limités, contre le tissu conjonctif, par une mince couche continue de cellules lamelleuses, formant une ou deux assises, parfois trois. Ces cellules possèdent un noyau plat, formé de chromatine dense; leur protoplasma est fortement colorable par l'éosine. La couche kératinisée suit très exactement le contour du cordon; quand deux cordons sont contigus, leurs membranes kératinisées se juxtaposent.

A un faible grossissement, cette couche marginale apparaît comme une mince bordure



rose; et sa continuité porte de prime abord à interpréter cette bordure comme une vitrée conjonctive, interprétation qu'un examen plus attentif ne justifie pas: dans une préparation colorée par la méthode trichrome de P. MASSON (hémalum—éosine—safran), les fibres conjonctives et les membranes vitrées sont, en effet, colorées en jaune.

Entre la zone reproductrice et la couche kératinisée périphérique, il existe souvent une ou deux rangées de cellules de transition, analogues à celles décrites autour de l'amas kératinisé intérieur.

La surface externe de la couche kératinisée est généralement lisse; parfois cependant



FIG. 4.—Même préparation—Grossissement du dessin 350  
Au centre du dessin, amas de débris cellulaires kératinisés (cordon spontanément stérilisé), que n'entoure aucune cellule néoplasique vivante.  
En haut et à gauche la surface d'un lobule est vue obliquement, de sorte que les squames kératinisées se présentent à plat. Près du même point, du sang a fait irruption dans un espace (non pourvu d'endothélium, et par conséquent de nature non-vasculaire) interposé entre le tissu conjonctif et la surface du lobule.

quelque squame se soulève, comme pour se détacher. Fait remarquable, cette surface n'adhère absolument jamais au tissu conjonctif, comme c'est au contraire le cas au niveau des membranes basales ou vitrées. Souvent même, une rétraction s'est produite entre le tissu conjonctif et la surface du cordon ou lobule; et ces deux tissus sont séparés par une fente. Tantôt cette fente est vide; tantôt elle est remplie par du sang, dont on voit la fibrine coagulée et les globules. On pourrait se demander si le système cordonal lobulé, possédant un revêtement corné si spécial, ne se développe pas dans un réseau de vaisseaux lymphatiques. Mais les vaisseaux lymphatiques (qui ne subissent jamais d'accroissement dans un tissu envahi par une tumeur maligne) n'ont pas—à beaucoup près!—dans la région du col utérin un développement comparable à celui du système cordonal lobulé en question. D'ailleurs la fente péri-lobulaire se distingue parfaitement d'un vaisseau sanguin ou lymphatique, par l'absence d'endothélium.

Il y a dans cet épithélioma, comme dans presque tous les épithéliomas épidermoïdes, une alternance très nette dans le développement des cordons. Les plus jeunes cordons (formés sans doute par des bourgeons appendus à des cordons ou lobules plus âgés) sont caractérisés par l'absence de kératinisation centrale, par les noyaux serrés et à structure dense de leur zone reproductrice. A un stade plus avancé, les cellules actives, quoique n'acquérant jamais des contours parfaitement distincts, s'agrandissent, se chargent de fibres colorables par l'éosine et leur noyau devient vésiculeux. Les cordons âgés possèdent un amas kératinisé intérieur gros, entouré d'une mince couche de tissu actif. Au dernier stade de leur évolution, les cordons ne sont plus représentés que par des résidus cornés, nus dans le tissu conjonctif, et s'y dissolvant sans intervention de leucocytes (Fig. 4).

*Tissu conjonctif et leucocytes.*—Les travées intercordinales sont formées de tissu conjonctif fibreux adulte. On y trouve des fibres collagènes, ordonnées en groupes parallèles, avec des fibroblastes typiques.

Il y a dans le tissu conjonctif intercordinal extrêmement peu de cellules mobiles: les polynucléaires sont complètement absents; les lymphocytes sont rares. On voit quelques petits groupes de plasmocytes. On ne trouve absolument aucun leucocyte dans les cordons et lobules, ni dans le tissu reproducteur, ni dans les amas kératinisés intra-lobulaires. Et ce caractère négatif contraste remarquablement avec l'abondance ordinaire d'une population leucocytaire variée dans les épithéliomas épidermoïdes habituels.

Dans la muqueuse du canal cervical (sur l'un des bords de la préparation histologique), la proportion des leucocytes et des plasmocytes, et la diapédèse des polynucléaires à travers les parties non cancérisées de l'épithélium pavimenteux stratifié sont, au contraire, normales.

Les vaisseaux sanguins sont représentés par des artérioles et des capillaires, dont beaucoup ont en coupe transversale une forme irrégulière et sont d'un calibre plus grand que celui de capillaires normaux. Ces vaisseaux se trouvent exclusivement dans le tissu conjonctif: on ne voit pénétrer dans les cordons et lobules épithéliomateux aucun bourgeon vasculo-conjonctif.

On rencontre quelques tubes glandulaires, qui ont la structure des glandes du col utérin. Il n'existe pas de signes de substitution du tissu épidermique cancérisé au tissu glandulaire.

Nous n'avons jusqu'à présent étudié, pour y rechercher cette anomalie histologique, que soixante-quinze épithéliomas pavimenteux du col de l'utérus, pris au hasard parmi un millier (environ) de cas traités à la Fondation Curie de 1919 à 1929 inclus. Sur les soixante-quinze cas examinés, nous avons trouvé six fois l'anomalie en question (soit 8 pour cent).

Voici de courts résumés des observations cliniques et radiologiques des cinq autres cas.

CAS II (XIV—A, n° 486).\* Si . . . , quarante ans.—Hystérectomie supra-cervicale pour fibromyome en 1922.—En janvier 1925: tumeur ulcérée occupant le col, les culs-de-sacs vaginaux antérieur et gauche; invasion bilatérale du paramètre; utérus bloqué; infiltration de la cloison vésico-vaginale, avec ulcération de la vessie.—Degré IV.

*Histologie:* épithélioma épidermoïde, disposition cordonale-lobulée; évolution cornée péri-lobulaire.

*Röntgenthérapie* du 13 janvier au 10 mars 1925.

Décès 27 octobre (survie sept mois et demi).

CAS III (XIV—A, n° 496).\* Bor . . . , quarante-deux ans. En février 1925 grosse

\* Observations clinique et radiologique du Dr H. COUTARD.

tumeur du col utérin, remplissant le vagin, ulcération des culs-de-sacs antérieur et droit; tumeur du paramètre droit, induration du paramètre gauche; utérus bloqué.—Degré III.

*Histologie:* épithélioma épidermoïde, disposition architecturale variable; évolution cornée ordinairement centrifuge, au contact du tissu conjonctif.

*Röntgenthérapie* du 19 février au 5 mars 1925, abandonnée en raison du mauvais état général.

Décès le 2 juin (survie trois mois).

CAS IV (XIV—A, n° 560).† Au . . . , quarante-huit ans.—Hystérectomie pour tumeur maligne du col le 10 août 1923. En novembre 1925: ulcération avec induration étendue du fond du vagin; signes d'envahissement de la vessie; bloc néoplasique unissant le fond du vagin à la paroi pelvienne des deux côtés.—Degré IV.

*Histologie:* épithélioma épidermoïde, disposition cordonale-lobulée; évolution cornée presque partout péri-lobulaire.

*Curiethérapie* du 5 au 11 novembre 1925; irradiation seulement extérieure, bientôt interrompue par le mauvais état général et la fièvre.

Décès le 15 octobre 1926 (survie onze mois).

CAS V (XIV—A, n° 738).\* Mar . . . , cinquante-trois ans.—Hystérectomie supracervicale pour fibromyome en 1925. Ulcération du col, sans induration des culs-de-sacs, ni du tissu conjonctif pelvien.

*Histologie:* épithélioma épidermoïde, disposition cordonale-réticulée. Evolution cornée péricordale.

*Premier traitement, curiethérapie vaginale* du 23 au 28 juin 1927.

Récidive locale constatée le 17 avril 1929.

*Deuxième traitement, curiethérapie vaginale* du 14 au 19 mai 1929, puis *röntgenthérapie* du 24 mai au 8 juin 1929.

Guérison douteuse (janvier 1930).

CAS VI.‡ Luc . . . . soixante ans.—Induration générale du fond du vagin; tumeur de l'isthme utérin; induration du paramètre gauche, avec rétraction de l'utérus de ce côté.—Degré II.

*Histologie:* épithélioma épidermique, à évolution épidermoïde seulement ébauchée; disposition cordonale-lobulée; lyse centro-cordale avec formation de cavités intra-épithéliales; kératinisation péri-lobulaire fréquente avec formation de squames au contact du tissu conjonctif.

*Traitement radiothérapique combiné* par curiethérapie intérieure et par rayons X, du 2 avril au 1er mai 1929.

La symptomatologie des six cas que nous avons observés ne présente aucun caractère spécial. Le nombre des cas étudiés est trop petit, et ces cas présentaient des degrés d'extension trop inégaux, pour qu'il soit possible de se faire une opinion sur la radiosensibilité de cette variété, comparative-ment à d'autres.

L'intérêt de cette variété d'épithélioma du col utérin est donc confiné actuellement à l'histologie pathologique. A cet égard, les faits principaux se résument ainsi:

(1) Dans les six cas étudiés, les situations relatives de la couche germinale ou reproductrice du tissu épithéliomateux et de sa couche stérile sont inversées

† Observation clinique et radiologique du Dr O. MONOD.

\* Observation clinique et radiologique des Drs G. RICHARD et J. PIERQUIN.

‡ Observation clinique et radiologique du Dr G. RICHARD.

par rapport à l'état de choses habituel. La couche germinale, au lieu d'être en contact avec le tissu conjonctif et à proximité du réseau capillaire sanguin, est séparée du milieu nourricier par la couche stérile des cellules en voie de kératinisation, ou déjà transformées en squames cornées. Quelquefois (dans deux de nos six cas), l'évolution cornée se fait à la fois vers la périphérie et vers le centre des cordons. Nous avons recherché soigneusement la pénétration possible de vaisseaux capillaires dans les cordons: nous ne l'avons jamais constatée. Par conséquent nous devons admettre que, dans cette variété d'épithélioma, la nutrition du tissu néoplasique s'effectue par diffusion du plasma à travers la couche stérile, en sens inverse des conditions habituelles.

Cette inversion du sens habituel de la transformation des cellules épidermiques et du courant nourricier qui alimente leur couche germinale n'est pas, dans nos observations, un phénomène accidentel n'intéressant que de petits territoires d'un lobule épithéliomateux. C'est un phénomène régulier; il intéresse la plus grande partie du tissu néoplasique, et il peut se généraliser à toute l'étendue du système cordonal-lobulé qui constitue ce tissu. On le retrouve sous modification dans toutes les parties du tissu de la récidue (cas I, rapporté en détail). Nous devons conclure de cela que, dans un épiderme, la transformation des cellules aboutissant à la formation de squames stériles ne résulte pas du fait que les couches successives de cellules s'éloignent de plus en plus du milieu nourricier. Nous montrons, en effet, que cette transformation n'est pas empêchée lorsque les cellules les plus anciennes sont en contact avec le tissu conjonctif. L'évolution cornée des cellules épidermiques paraît être la manifestation d'une propriété inhérente à ces cellules.

(2) L'interposition anormale d'une couche continue de squames cornées entre le milieu vasculo-conjonctif et le tissu fertile de l'épithélioma épidermoïde semble empêcher la pénétration des leucocytes dans le tissu épithéliomateux.

Il y a des cas, il est vrai, où la population leucocytaire de la tumeur est extrêmement clairsemée, le tissu conjonctif intercordonal étant presque désert (exemple: cas I décrit en détail). Mais dans d'autres cas, au contraire, les espaces conjonctifs sont abondamment peuplés de lymphocytes et de plasmocytes. Toujours les leucocytes ont été trouvés en nombre extrêmement minime dans les cordons épithéliomateux, ou même ils en étaient tout à fait absents. Jamais il n'a été trouvé d'amas de leucocytes au contact de la couche cornée qui revêt la périphérie des lobules. Cela porte à penser d'une manière générale, que les leucocytes ne jouent pas un rôle indispensable dans la transformation cornée des cellules épidermiques.

(3) Dans la plupart des variétés histologiques des épithéliomas épidermoïdes, on peut constater une alternance de stades entre les diverses parties du système cordonal-lobulé qui les constituent. Les cellules germinales à corps protoplasmique encore incomplètement individualisé, les cellules polyédriques, les cellules à éléidine (quand elles existent), les cellules en

cours de kératinisation, les squames ayant achevé leur évolution ne se succèdent presque jamais régulièrement en tous les points du système cordonal-lobulé: la composition cellulaire est alternante d'un point à un autre. Dans la variété que nous avons décrite, cette alternance est nette. Le stade le plus jeune est représenté dans le système cordonal-lobulé par des régions intérieures, dont la structure est syncytiale, et où les noyaux sont petits, serrés les uns contre les autres et riches en chromatine. Le stade ultime est représenté par des amas de squames (cas I), ou bien par des squames isolées les unes des autres (cas III) dans le tissu conjonctif.

#### RÉSUMÉ

Nous décrivons dans cet article les particularités histologiques d'une variété d'épithélioma du col de l'utérus, que nous dénommons: épithélioma pavimenteux stratifié, à évolution épidermoïde, à transformation cornée péricordale. Cette variété a été rencontrée dans 8 pour cent des cas d'épithélioma pavimenteux stratifié du col. Elle ne paraît pas présenter de caractères particuliers dans son évolution clinique. On ne peut encore rien dire de sa radiosensibilité.

## IV

RADIUM AND RÖNTGEN RAY THERAPY

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in the University of London.
- "The Experimental Use of a Large Quantity of Radium in Treatment."
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- "Interstitial Radiation in Metastatic Cervical Nodes of Epidermoid Carcinoma."
- LLOYD F. CRAVER, M.D.      New York, N. Y.  
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- "A Case of Malignant Thymic Tumor, Probably Carcinoma, Treated by Heavy Irradiation; With a Report of Autopsy Findings."
- RALPH E. HERENDEN, M.D.      New York, N. Y.  
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- "The Röntgen-ray Treatment of Giant Cell Tumors of Bone."
- GEORGE E. PFAHLER, M.D.      Philadelphia, Pa.  
Professor of Radiology, University of Pennsylvania.
- "Röntgen Therapy in Carcinoma of the Breast; A Statistical Study of 977 Private Cases."
- HERMAN WINTZ, M.D., PH.D.      Erlangen, Germany  
Director of the Woman's Clinic, University of Erlangen.
- "Discussion of the Results Obtained with Carcinoma Uteri Treated by Röntgen Rays from 1915 to 1925."
- CURTIS F. BURNAM, M.D.      Baltimore, Md.  
Associate Professor of Gynecology, Johns Hopkins Hospital.
- "The Treatment of Cancer of the Body of the Uterus by Radiation."
- JAMES HEYMAN, M.D.      Stockholm, Sweden  
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- "Experiences with Combined Radium and Roentgen Treatment of Cancer of the Cervix Uteri at Radiumhemmet, Stockholm."
- WILLIAM P. HEALY, M.D.      New York, N. Y.  
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- "The Treatment of Carcinoma of the Cervix Uterus."
- ANTOINE LACASSAGNE, M.D.      Paris, France  
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- "Les Metastases des epitheliomas du col uterin localement gueris par radiotherapie."
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- "How Far Can Radium Replace Radical Surgery for Cancer of the Rectum?"
- J. E. GENDREAU, M.D.      Montreal, Canada  
Director of the Radium Institute of Montreal.
- "Far Reaching Effects of Gamma Rays and Short X-ray Upon the Human Heart."

# THE EXPERIMENTAL USE OF A LARGE QUANTITY OF RADIUM IN TREATMENT

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THE idea that if a given agent be beneficial in small quantities it will be more beneficial in large is ingrained in human nature. Hence it was only reasonable to expect an attempt to utilize large quantities of radium in the treatment of cancer, soon after it became evident that the small quantities hitherto available afforded results that were beneficial to an astounding extent. Between August, 1919, and August, 1920, such an attempt was made at the Middlesex Hospital, London, with a quantity of hydrated radium bromide amounting to nearly five grams (representing about two and a half grams of the element) that was lent to the hospital by the Medical Research Council. In due course an account of the various investigations conducted was published under the title of "The Medical Uses of Radium" (Medical Research Council, Special Report, Series No. 62, 1922).

On some of the more definitely histological investigations the report was extensive, but the results of the therapeutic inquiry did not seem to call for description in detail. Since, however, treatment with large quantities of radium, later, was examined in the Radium Institute, Paris, and is now being conducted at the Westminster Hospital with four grams of radium element lent for the purpose by the National Radium Commission of Great Britain it seems that a detailed account of a somewhat similar experiment carried out ten years ago would be of use to those now engaged in the work.

The inquiry at the Middlesex Hospital was in the nature of team-work. The patients were under the care of the physicians and surgeons of the hospital; the physical determinations were carried out by Professor Sidney Russ; the blood examinations and some of the clinical observations were made by Dr. Helen Chambers; and, in the main, I was responsible for the actual treatment and the clinical notes. For the present paper and for any opinions advanced therein I am alone responsible. Although I have now retired, they are based upon the detailed records made at the time of the experiment, to which I have access by the kindness of the authorities of the Middlesex Hospital.

*The physical material.*—Considerations of technic and the experimental basis for therapeutic work are considered in some detail in the Medical Council's Report to which reference has been made. Here it will suffice to say (1) that gamma radiation was used; (2) that the radium was contained in a circular brass box 11.7 centimetres in diameter; (3) that the radium box was placed as close as possible to the part to be irradiated short of actual



contact; (4) that an exposure of approximately eight hours under the conditions in (3) was necessary to prevent Jensen rat sarcoma cells from growing when subsequently inoculated into normal animals; (5) that a continuous irradiation of four to five hours was regarded as the limit which the human skin would tolerate; (6) that such an exposure was unlikely to be lethal to the cancer cells, particularly at a depth, and (7) that the production of a radium burn was of inferior importance to the attempt at influencing the disease beneficially.

*The duration of exposure.*—Of the 108 cases considered here, seventy-seven received a single exposure that lasted as a rule four hours if only one site was irradiated or five or six hours if more than one region (*e.g.*, front and back, both sides of thorax) was treated. An exposure was divided into two or three portions in order to allow intervals for food and rest. Twenty cases received two exposures at an interval of a fortnight upwards according to circumstances, the total duration of exposure being generally between eight and eleven hours. In six cases the patient received three exposures at intervals but the total duration of exposure was again generally eight to eleven hours. In four cases the patient received four exposures at intervals and the total duration of exposure varied greatly, being eight, twelve, sixteen and twenty-one hours, respectively. In one case (lymphosarcoma of thorax and neck) the patient received six exposures, lasting in all twenty-three hours. In most cases of repeated exposure a second or subsequent exposure was given because the improvement noted after the first exposure was not maintained. In a few, the exposures were given with an interval of less than a fortnight in the hope of producing a lethal effect on the neoplastic cells by summation of irradiation. In all such cases, however, one was handicapped by the great probability of producing a severe radium burn.

*The clinical material.*—Inasmuch as it seems desirable for our present purpose that the amount of radium under consideration should be constant and as some of the radium was removed from the brass container from time to time at a later date in order to prepare tubes containing small quantities and radium needles, the number of cases analyzed here is less than that contained in the Medical Research Council Report (*i.e.*, 168). In the present paper 108 cases are included; in some, the information is meager but all cases treated during the period are presented without omission. With few exceptions the treatment was undertaken for malignant disease and usually the disease was in a very advanced stage; in such an experiment it was felt that it was only justifiable when no other recognized form of treatment was possible.

On examination the results in the present smaller number of cases agree in the main with those contained in the list given in the Medical Research Council Report. The only difference of importance arises in connection with cases of cancer affecting the breast. Thus a discrepancy occurs between the present and the Medical Research Council Report in respect to the ultimate results of cases, due in large part to information received subsequent

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to the publication of that report. In the present series of thirty-seven breast cases it is known that at least twenty-eight deaths occurred (*i.e.*, 76 per cent.), whereas the number of deaths in the entire series of seventy-eight breast cases contained in Table II of the Medical Research Council Report is only twenty-four (*i.e.*, 31 per cent.). The fact supports once more the contention that early reports of results in cases of cancer are dangerous particularly when cancer of the breast is under consideration.

For our present purpose the cases at our disposal are grouped in three ways: (A) The whole series of 108 cases is considered in respect of certain immediate or early constitutional and local effects. (B) The 108 cases are subdivided into seven classes, *viz.*, breast, thirty-seven cases; tongue, and mouth, including neck to œsophagus, twenty-six cases; rectum, six cases; skin including lip, seven cases; malignant disease at sites not included above, twenty cases; lymphadenoma, lymphosarcoma and leukæmia, nine cases; other conditions, three cases. (C) A comparison is made between growths that were certainly or probably sarcomatous, twenty-six cases, and growths that were certainly or probably carcinomatous, seventy-three cases.

(A) *Immediate or early constitutional and local effects. The blood.*—It was thought that blood examination might afford some indication of the radium action and in forty-two cases examinations were made before irradiation and as far as possible on the second and seventh days after irradiation. The actual findings are given in the Medical Research Council Report; here they are summarized and the means alone are given below:

### *Means of All Cases of Blood Examination*

#### Males, 22 Cases

|                                | Hæmo-<br>globin | Hæmo-<br>globin<br>index | Red<br>blood-cells | White<br>blood-cells | Neutro-<br>philes<br>per<br>cent. | Lymph-<br>ocytes<br>per<br>cent. | Large<br>mono-<br>nuclears<br>per<br>cent. |
|--------------------------------|-----------------|--------------------------|--------------------|----------------------|-----------------------------------|----------------------------------|--|
| Before radiation.....          | 88.8            | 89.3                     | 4,973,000          | 18,400               | 72.1                              | 23.3                             | 3.1  |
| Two days after radiation.....  | 87.5            | 88.6                     | 4,935,000          | 16,650               | 75.0                              | 20.1                             | 3.9  |
| Seven days after radiation.... | 87.3            | 85.7                     | 5,094,000          | 15,000               | 69.8                              | 24.3                             | 5.0  |

#### Females, 20 Cases

|                                | Hæmo-<br>globin | Hæmo-<br>globin<br>index | Red<br>blood-cells | White<br>blood-cells | Neutro-<br>philes<br>per<br>cent. | Lymph-<br>ocytes<br>per<br>cent. | Large<br>mono-<br>nuclears<br>per<br>cent. |
|--------------------------------|-----------------|--------------------------|--------------------|----------------------|-----------------------------------|----------------------------------|--|
| Before radiation.....          | 86.8            | 81.2                     | 5,348,000          | 13,200               | 67.0                              | 27.6                             | 4.4  |
| Two days after radiation.....  | 81.4            | 77.9                     | 5,228,000          | 12,770               | 72.9                              | 22.4                             | 3.7  |
| Seven days after radiation.... | 80.1            | 76.9                     | 5,207,000          | 11,400               | 71.0                              | 22.1                             | 6.0  |

That the foregoing represents the facts with fair accuracy is shown by the means afforded by twenty-six cases (fourteen males, twelve females) in each of which the entire series of three observations was available.

From these observations we may conclude that exposure to the gamma rays of a large quantity of radium causes a diminution in the numbers of erythrocytes and leucocytes from the first; that the hæmoglobin and

|                                | Hæmo-<br>globin | Hæmo-<br>globin<br>index | Red<br>blood-cells | White<br>blood-cells | Neutro-<br>philes<br>per<br>cent. | Lymph-<br>ocytes<br>per<br>cent. | Large mono-<br>nuclears<br>per<br>cent. |
|--------------------------------|-----------------|--------------------------|--------------------|----------------------|-----------------------------------|----------------------------------|---|
| Before radiation.....          | 85.9            | 83.3                     | 5,154,000          | 17,150               | 73.2                              | 24.0                             | 2.9                                     |
| Two days after radiation.....  | 85.9            | 83.9                     | 5,115,000          | 15,740               | 74.9                              | 20.2                             | 3.9                                     |
| Seven days after radiation.... | 82.8            | 81.3                     | 5,092,000          | 14,230               | 69.4                              | 23.9                             | 5.8                                     |

hæmoglobin index undergo a progressive decline during the week after exposure; and that there occurs an alteration in the relative percentages of neutrophile cells, lymphocytes and large mononuclear cells indicating an early destruction of lymphocytes and a progressive increase in the number of large mononuclear cells. These results are in accord with observations made on the blood in experimental animals and determined histologically (see Medical Research Council Report, pp. 46, 58, 85, 98, 108, 113).

*Vomiting and nausea.*—In eight cases vomiting was noted during or shortly after the radium exposure and in a few other cases there was some degree of nausea without vomiting. The vomiting was often severe and lasted for several days. It seemed to be dependent upon radiation effects upon the stomach itself for in all but one case (perineal irradiation) the stomach must have received an appreciable amount of gamma radiation from its proximity to the primary region of treatment. It must be conceded, however, that in many other cases in which the conditions of radiation were apparently identical, no vomiting or nausea occurred.

*Erythema and dermatitis.*—Thirty-nine cases showed a greater or less degree of skin implication by the radium rays. Eighteen cases developed a severe radium burn of the usual character and owing to the large area of irradiation such a burn was often nearly as large as the palm of the hand, deep, persistent and showing little inclination to heal. In thirteen additional cases there was a severe but more superficial dermatitis and in eight more there was erythema which ended in bronzing of the skin. The effects seemed to be due to the gamma radiation, for in one case in which half the area to be irradiated was covered with a sufficiency of oiled silk to exclude secondary beta rays, no difference was observed in the subsequent dermatitis over the protected and unprotected areas.

*Other local results.*—Local oedema occurred in five cases and was spread over a far greater area than the diameter of the radium capsule. A spreading septic cellulitis which started in the irradiated area and was rapidly fatal occurred in two cases. Local hæmorrhage occurred in four cases. Degenerative changes leading to softening and evacuation of pus-like material from a hitherto solid mass occurred in five cases and increase in the area of ulceration in six cases; an enhancement of the foul condition of the mouth was noted in four cases of cancer affecting this part and probably is of the same character. In nine cases the local pain was diminished; in eight it was increased.

*The region of disease.*—In forty-four cases there was an early improvement in the irradiated region of disease as determined by inspection aided often by periodic measurements and photographs. Sometimes this improvement was remarkable and in eleven cases which had been deemed inoperable before exposure to radium the subsequent condition was such that surgical removal of the mass was undertaken (breast, seven; supraclavicular glands, one; sarcoma of tibia, one; sarcoma of thigh, one; carcinoma of calf, one. But with very few exceptions such improvement was of short duration; occasionally a second, or even a third irradiation was followed by a certain amount of improvement, but as a rule rapid extension occurred until death. Even of the eleven cases mentioned above as having undergone surgical removal of the mass, the final results dated from the first radium exposure were as follows. Breast cases: death occurred in five cases in nine and a half, fifteen, fifteen, seventeen and twenty-three months respectively, and two cases were lost sight of in good health after eight and sixteen months respectively. The sarcoma of tibia case died ten months and that of sarcoma of thigh thirty months after the first exposure to radium while the carcinoma of calf case was alive and well four years after the first irradiation and that of cancerous supraclavicular glands was alive and well six and a quarter years after the first irradiation. Of the remaining thirty-three cases in which local improvement was recorded after the initial irradiation, twenty-two died and six were lost sight of within twelve months of the first radium treatment, two died within eighteen months, two breast cases and a case of chronic adenitis of the neck were alive and well when lost sight of respectively seventy-five, seventy-six and forty-five months after the first radium treatment.

(B) *Cases considered according to the site of the disease. Breast (thirty-seven cases, all malignant).*—Of the thirty-seven cases, twenty-seven, or 73 per cent., either died in hospital or returned to their homes to die. The period intervening between the first exposure to the large quantity of radium varied between a few days and three years; in ten cases it was nothing to six months, in eleven cases seven to twelve months, in three cases twelve to eighteen months and in the three remaining cases death occurred at twenty-three, thirty-five and thirty-six months, respectively. The first irradiation was separated from death by a mean period of ten months; in this connection it may be remembered that the mean duration of untreated cancer of the breast from the reputed date of onset to death is approximately thirty-nine months. Concerning the remaining ten cases that were lost sight of short notes are given below.

- (1) Amputation after irradiation: lost sight of eight months after one exposure of four and three-quarter hours. Last note: "Recurrences in skin and axilla."
- (2) Recurrence in skin, axilla, supra- and infraclavicular spaces: lost sight of nine months after the first of two exposures totalling seven and a half hours. Last note: "Extension of disease but health fair."

- (3) A single recurrence in skin after operation: lost sight of ten months after one exposure of three hours. Last note: "No sign of nodule, feels well."
- (4) Recurrence seven years after operation: lost sight of twelve months after one exposure lasting five hours. Last note: "In fair general health."
- (5) Breast, axilla, sternum: lost sight of fifteen months after one exposure of four hours. Last note: "Breast growth quiescent."
- (6) Breast, axillary and supraclavicular glands, eight years' duration: lost sight of sixteen months after two exposures, totalling eight and a half hours. Last note: "Growth quiescent, no supraclavicular growth, doing her work."
- (7) Duct carcinoma (operable), amputation six weeks after one exposure lasting five hours: lost sight of four years after radium exposure. Last note: "In good health."
- (8) Breast (operable), amputation one month after one exposure lasting three and three-quarters hours: lost sight of four and a quarter years after radium exposure. Last note: "Apparently well."
- (9) Recurrences (seven years after operation) in supra- and infraclavicular spaces: lost sight of six and a quarter years after one exposure lasting five and a half hours. Last note: "No signs of recurrence."
- (10) Recurrence in supraclavicular space: lost sight of six years and four months after the first of two exposures totalling nine and a half hours. Last note: "No recurrence detected; in good health."

Of these cases Nos. 7, 8, 9 and 10, I think, may fairly be claimed as satisfactory though how far the result is to be ascribed to action of the radium cannot be determined.

One case in the group which terminated fatally is of peculiar interest in the present connection. Prior to the final admission to hospital the patient had suffered from a cancerous ulcer of one breast which healed completely under X-ray treatment; on admission she had a similar ulcer in the other breast and this under three exposures to the large quantity of radium totalling twelve hours improved very considerably, cicatrization taking place around the edges. Later the ulcer became indolent and finally the growth extended. She died eighteen months after the first exposure. The beneficial effect of X-rays and later of gamma rays upon two separate cancer masses raises the question whether a constitutional condition existed in this patient which enabled her to react to irradiation in an unusually favorable manner. It is undoubted that of two cases apparently similar the one may react well, the other badly, to the same degree of irradiation, so that the existence of a constitutional factor in determining the result seems to be possible.

*Tongue and mouth, neck, œsophagus (twenty-six cases, all malignant).—* Of the twenty-six cases all but one are known to have died from their disease. The mean duration of life in the twenty-five cases that died was

3.7 months from the first exposure to radium. In seven of the cases there was a temporary local improvement, in six there was no recognizable change, in eleven a definite change for the worse was recorded. The surviving case was that of a man who received one exposure of two hours before partial removal of tongue and glands and seventy days later an exposure of two and a quarter hours. He was lost sight of four years and seven months after the first exposure; last note: "No recurrence, fairly well."

*Rectum (six cases, all malignant).*—Death occurred in all, on an average of 5.6 months after the first exposure to radium. Three of the cases developed severe radium burns over the sacrum. Relief of pain was recorded in three cases but otherwise no benefit was discernible.

*Skin including lip (seven cases, all malignant).*—Six cases died on an average of six and a quarter months after the first exposure to radium; two of these showed a temporary improvement. The seventh case was that of a man with a large fungating carcinoma of the calf. He was lost sight of four years after one exposure of five hours which was followed by so great a diminution of the growth that it was removed surgically a month later.

*Malignant disease at sites other than those mentioned above (twenty cases).*—The sites of disease were parotid, four; cervix uteri, two; colon, two; bone, four; abdomen, chest, prostate, testicle, bladder, stomach, thigh, lung, one each. Of the twenty cases seventeen are known to have died and with the exception of two cases to which reference is made below the mean duration of life after the first exposure was 3.4 months. One case was lost sight of nine months after the first exposure: "worse," one after twelve months: "condition unchanged," and in one the result was entirely doubtful owing to absence of record. Four cases showed a temporary diminution in size of the growth or other improvement but in the remainder there was nothing noteworthy. Two cases that ended fatally were remarkable for their length of survival, the first being that of a man with sarcoma of testicle who lived three years and two months after one exposure of four and a half hours to the large quantity of radium, the other being that of a man with a large sarcoma of thigh who lived two and a half years after four hours' irradiation and subsequent surgical removal of the mass.

*Lymphadenoma, lymphosarcoma, leukæmic conditions (nine cases).*—In all the cases in this group there was enlargement of lymphatic glands or spleen or both. In one case the result is entirely doubtful owing to lack of record. The remaining eight cases died, respectively, three days, ten days, fourteen days, four months, four and a half months, seven months, nineteen months and forty-two months after the first exposure to the large quantity of radium. Two cases are worthy of further remark.

CASE I.—A medical man admitted apparently moribund with pronounced lymphosarcoma of neck and thorax. The first exposure, lasting three hours, was followed by so great a relief that further exposures of three and a half hours, two and a half hours and three hours were given over various sites of neck and thorax during the next three days. Sixteen days after admission he left London for his home in Northern Ireland

in a very fair condition but two months later, the condition having reverted, he returned to London for further radium treatment with the large quantity. Two exposures of five and six hours respectively were given within twelve days and again the improvement was remarkable. Once more he returned home but the condition rapidly became worse and he died four months after the first exposure to radium.

CASE II.—Lymphatic leukæmia with enlarged spleen and glands in both groins. In this case the changes produced in the numbers of red and of white blood-cells by a single exposure lasting five hours over the splenic area were determined daily at 5 P.M. by the same skilled observer using the same instruments. They were as follows:

|                                  | Before irradiation | Immediately after irradiation | Day 1     | Day 2     | Day 3     | Day 4     | Day 5     | Day 7     |
|----------------------------------|--------------------|-------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
| Erythrocytes.....                | 3,040,000          | 1,831,000                     | 1,508,645 | 1,415,625 | 1,716,250 | 1,956,250 | 1,884,375 | 2,262,500 |
| Leucocytes.....                  | 326,708            | 219,687                       | 67,937    | 98,437    | 35,000    | 36,250    | 52,187    | 59,375    |
| Neutrophils per cent. ....       | —                  | 1                             | 1.5       | —         | —         | —         | 1         | 1         |
| Lymphocytes per cent. ....       | 55                 | 96                            | 92        | 73.5      | 63        | 92        | 11        | 95        |
| Large mononuclears per cent. ... | 45                 | 3                             | 6.5       | 26.5      | 37        | 8         | 88        | 4         |

On the fourth, fifth and seventh days, it was uncertain whether cells should be classed as lymphocytes or large mononuclear cells; they were smaller than large mononuclears in earlier specimens but definitely larger and less deeply stained than lymphocytes.

*Other conditions (three cases).*—Of these cases one with chronic adenitis of neck was lost sight of apparently quite well three years and nine months after one exposure lasting five and a quarter hours; one with keloid over the site of a former mastoid operation was lost sight of, unimproved, thirteen months after one exposure lasting three hours, and one suffering from a sub-sternal mass of doubtful nature was lost sight of in a worse condition eighteen months after the first of three exposures, lasting in all ten and a quarter hours.

(C) *Comparison between sarcomatous and carcinomatous cases.*—For this comparison there are available twenty-six cases that were certainly or probably sarcomatous and seventy-three cases that were certainly or probably carcinomatous. This section may be dismissed shortly for the mean duration of life of the twenty-three fatal sarcomatous cases after the first exposure was seven and a half months and the mean number of exposures was 1.5, while in the fifty-nine fatal carcinomatous cases the corresponding numbers were seven and a quarter months and 1.4 exposures. These differences have no significance. On the other hand there is no case in the sarcoma group parallel to the six cases (four, breast; one, skin of calf; one, tongue) in the carcinoma group that were free from growth and in good health at periods varying from four to over six years after the first exposure to the large quantity of radium and then were lost sight of.

*Discussion.*—There can be no doubt concerning the potency of a large quantity of radium when used in treatment; the definite and rapid effects manifested by the blood, the dermatitis amounting often to a severe radium burn, the occasional rapid diminution in size of a mass of growth and the

vomiting that sometimes follows on the exposure are sufficient evidence of the fact. But whether the advantages outweigh the disadvantages is a more difficult question. In my opinion there is little doubt. In spite of the fact that the cases used for experiment were mostly in the latest stages, in spite of the favorable results noted in a few, I cannot but recall the similar experiences when radium therapy was in its infancy and only small quantities of the element were used. The beneficial results noted in the cases under present examination should, I think, be ascribed to radium action as such, apart from the quantity used; the large quantity employed and its nearness to the patient are, in my opinion, accountable for nothing but the grave disadvantages that occurred. Whether use of a large quantity of radium at a greater distance and over longer periods, thus approaching more towards the modern method of prolonged treatment with radium needles and radon seeds, would be efficacious, the present experiments do not indicate. From the financial and technical points of view provision of quantities of radium sufficient to be useful would be formidable. The falling off in intensity of gamma radiation owing to distance and the number of patients to be treated are of an order to increase the difficulties enormously. Were there evidence from the present investigation that the results of such treatment would be outstandingly good, no doubt these difficulties might be overcome; unfortunately, this is not the case.



# INTERSTITIAL RADIATION IN METASTATIC CERVICAL NODES OF EPIDERMOID CARCINOMA

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IN MAKING a general survey of the treatment of metastatic cervical nodes of epidermoid carcinoma at The Memorial Hospital, we have been impressed by the value of filtered radon implantation in certain of the cases. In view of the possibilities of this form of radium application, a brief discussion of the experiences to date seems to be in order.

A summary of the general plan of cervical-node treatment may indicate more clearly basis of case selection in group at present under discussion.

Since 1916 a conservative surgical plan in the treatment of cervical nodes in cases of intra-oral cancer, a course decidedly at variance with the generally accepted method of routine block dissection, has been followed. The premise that metastasis is by embolism rather than by direct permeation of lymphatics has been accepted. In the adult types of epidermoid carcinoma, at least, involvement of a single node only in the early course of the disease is the rule. With the more embryonal types, this may be followed by other nodes in rapid succession but if so the metastatic deposits tend to be generalized and not necessarily confined to the neck. We believe that up to a certain point at least cervical lymph-nodes perform a conservative function and hence should not be disturbed, if avoidable, particularly in the presence of an active primary growth. For these reasons *routine* dissections, either unilateral or bilateral, have not been resorted to. In the earlier course of the work, a complete unilateral dissection was done in all cases presenting a removable node. These dissections have always been done under local anæsthesia, the technic employed being as radical as possible and at the completion of the operation, and just before closing the wound, radium emanation has been buried at certain of the more dangerous points, particularly where the lymphatic paths were severed.

In the beginning of this work external radiation was very little employed. The unfiltered emanation in glass seeds, or, as they have been commonly called, "bare tubes," represented the only source of effective radiation, and it was coupled with operative surgery. As external radiation became more effective it was employed as a routine procedure in the treatment of all necks in intra-oral carcinoma, as a preliminary step in the treatment program. If no nodes were palpable, the case was kept under routine observation and no other therapeutic measures directed toward the neck. If a metastatic node or nodes, technically removable, were present upon admission or appeared subsequently, a complete dissection was done following the external radiation.

## RADIATION METASTATIC CERVICAL-NODE CANCER

If the metastatic mass was inoperable external radiation as a palliative measure was continued.

As technical facilities for X-radiation improved, and with added experience in more intensive external radiation dosage, more pronounced effects by way of growth restraint were noted. Certain of the cases showed a much more marked effect than others. Investigation, from a histological standpoint, of the reasons for this peculiar response to radiation in some cases has led to a much clearer understanding of the cellular types of epidermoid carcinoma. Observations on this point by Ewing have led him to apply the term "transitional-cell carcinoma" to a rather large group of the cellular



FIG. 1.—Recurrent metastatic neck. Note bulging recurrent mass at angle of mandible with skin fixation anteriorly over lower border of jaw. Heavy line indicates exposure incision by excision of old scar.

epidermoids showing a peculiar response to radiation. To a more limited group, Regaud and Schmencke have applied the term, "lympho-epithelioma."

It is not the purpose of this paper to discuss the histological characteristics of these tumors. The purpose is rather to call attention once more to the fact that recognition of these radiosensitive tumors as definite clinical entities was brought about through first noting their peculiarly favorable response to external radiation. Further clinical study shows that while these undifferentiated growths show a marked local response to radiation they tend to disseminate widely. The local process can be dealt with more certainly by radiation than by operation and, furthermore, the chance of controlling the disease completely by a neck dissection is not great enough to warrant the doing of it. Distant extension, once the cervical nodes are involved, is very apt to occur. Withdrawal of this group, therefore, from the operative class entirely, at once cuts down very considerably the number of neck dissections in our service.

For several years, radium emanation in the form of a radium emanation pack, which contained from 2,000 to 2,500 millicuries of emanation, in full erythema doses at distances of 6 and 10 centimetres was employed as far as possible. It is only during the past three and one-half years, however, since acquiring the four-gram radium element pack, that we have been able really adequately to carry out this external radium irradiation of the neck. This has added tremendously to the facility and accuracy of the treatment. During the same period there has been marked improvement in the technic of X-radiation. Furthermore, the work of Quimby and Pack has suggested that the combination of X-radiation and radium, externally, was more advan-

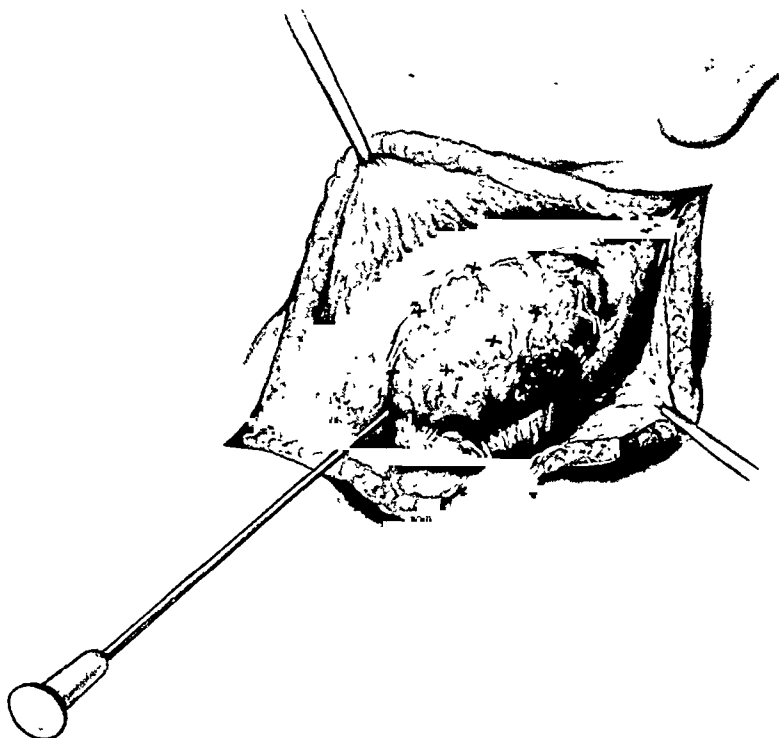


FIG. 2.—Gold tube radon implantation. Note area of necrosis at lower part of metastatic mass.

tageous, quantitatively at least, than the employment of one or the other agent alone. Clinical observations on the combined use of the two agents were responsible for initiating the experimental work of Quimby and Pack and have continued since to substantiate their observations.

At present, therefore, the lymph-node areas of the neck in every case of intra-oral cancer are radiated as promptly as possible after admission to the service. Following this initial irradiation of maximum intensity, unilateral neck dissections under local anæsthesia are done in cases of adult type epidermoid carcinoma presenting clinically involved unilateral nodes with intact capsules and in the presence of a primary growth either controlled already or

favorable from that standpoint. Bilateral involvement of nodes is considered an indication of inoperability. Perforation of the node capsule is an indication of inoperability. Dissection is not justifiable even in an otherwise operable neck unless the prospect for cure of the primary growth is a reasonable one. It occasionally happens that the patient's general physical condition, for one reason or another, will not permit of a complete unilateral dissection even though all local factors would place the case in that class. As previously stated, we regard the metastatic nodes of transitional-cell carcinomas, in fact all cellular epidermoids, as being more amenable to radiation therapy than to dissection.

The problem next arises as to how best to handle these various cases where dependence must be placed upon radiation in some form. A few of the most radiosensitive epidermoid carcinomas may be cleared up completely by external irradiation providing it is of the maximum intensity that the skin will stand. Assuming a total treatment interval of a month and preferably, perhaps, of a fortnight, not more than  $2\frac{1}{2}$  or 3 erythema doses of radiation—whether the most efficient high-voltage X-rays or heavily filtered radium at 6 to 10 centimetres' distance, or both—can be delivered to the lymph-node-bearing areas of the neck. This may take care of the occasional case of particularly radiosensitive character, but beyond this the most that can be hoped for at present is a variable degree of growth restraint.

These gross clinical observations are exactly in accord with the findings of Martin and Quimby in measuring the intensity of radiation in terms of skin erythema doses in a large series of intra-oral carcinomas, taking account of the radiation intensity both at the primary site and in the involved nodes. They have shown that in order to produce complete regression of the adult types of epidermoid carcinoma an intensity of 7 to 10 skin erythema doses is essential throughout the tumor-bearing area and that with the cellular undifferentiated epidermoid carcinomas, the minimum essential intensity varies from 3 to 5 skin erythema doses. Keeping these facts in mind, the problem at once arises as to how best to handle, by way of supplementing the external radiation, the varied group of metastatic nodes classed, for one reason or another, as inoperable. During the years in which unfiltered emanation was used for implantation, attempts were made upon numerous occasions to control otherwise inoperable nodes by direct implantation of bare tubes. In a very few instances the method was successful, but for the most part it failed because of the necrosis which almost invariably followed the use of radiation of this *quality*.

During the latter part of 1924, Failla made possible the collection of emanation in gold capillary tubes employing first a wall thickness of 0.2 millimetre of gold and very shortly changing it to 0.3 millimetre. We have had the advantage of using these filtered radon tubes for interstitial implantation for a full five years. It is this source of radiation which is now used to supplement to the desired intensity the radiation of inoperable metastatic cervical nodes.

Most of the cases treated have been of palliative character. A certain number, however, as will be noted from the cases assigned to this form of therapy, have, as far as the local process is concerned and viewed from a technical standpoint, been locally operable. This affords some basis at least for comparison, in a general way, with dissection. It is the opinion at present that this combined method of irradiation, with dependence upon filtered radon interstitially for bringing the intensity of radiation up to the desired point, offers a possibility for future improvement in the treatment of the metastatic cervical nodes of epidermoid carcinoma even though external irradiation remains for the most part at a standstill. The trend toward interstitial implantation in metastatic nodes has been gradual. The physical disadvan-

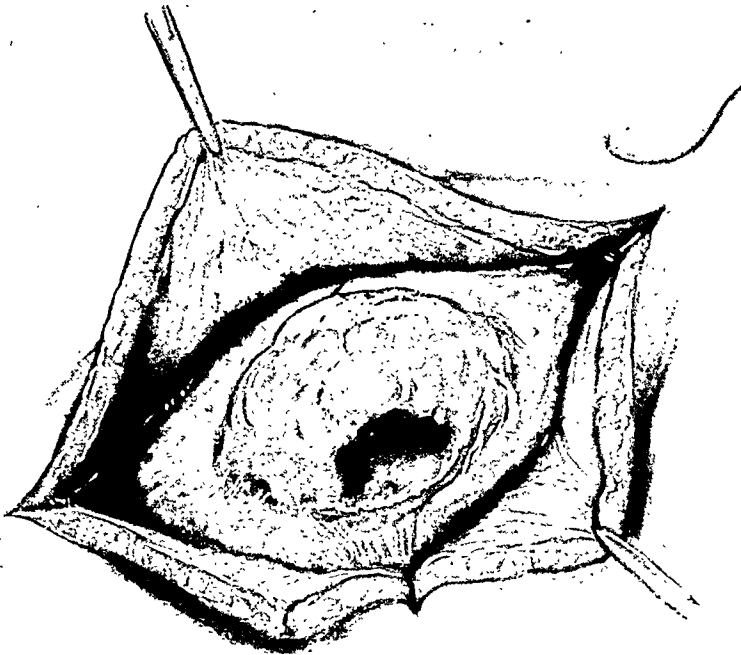


FIG. 3.—Showing necrotic portion of metastatic mass cleaned out preliminary to wound closure.

tages of the old bare tubes have to a large extent been overcome by the present 0.3 millimetre gold filtered radon tubes. Within reasonable limits, an adequate quantity of radiation can be delivered for local control of the growth. The extremely advanced, bulky metastatic nodes are not in a general way suited to treatment by interstitial implantation. As has been shown by Martin and Quimby, a point is reached in the size of the mass under consideration where the relative efficiency of interstitial implantation within the limits of tissue tolerance gives way to external distance irradiation. This is true in the very large, bulky masses of 6 to 10 centimetres or more in diameter, from a physical standpoint alone, and furthermore, there are various additional reasons for refraining from interstitial implantation in these bulky masses,

particularly the factor of blood supply to the tumor mass and the probability of a wide zone of central necrosis.

The technical procedure of filtered radon implantation is simple. It is done under local anæsthesia and without shock to the patient. While the method aims only at being a form of local treatment, the intensity of the radiation is such that it extends far beyond the limits of any possible local surgical removal. Through local control of a given node, growth is checked and complete or partial bulk regression is brought about. The tumor mass as a source of metastatic emboli is eliminated. Pain incident to the increasing size of an uncontrolled metastatic process is avoided. The broken down, foul, bleeding, fungating tumor masses characteristic of the late stages of uncontrolled metastatic disease in the neck are prevented. In certain of the more favorable cases a reasonable chance for complete control of the growth is offered. If an individual local metastatic process is controlled by this means, and we have proven repeatedly that it can be, then the patient's chance of a permanent result is as good as though that same mass had been removed by a wide margin at least. In making this statement we are not lending support in any sense to the local removal of metastatic nodes or to partial dissections. The fact remains, however, that with the clinical course of the more adult types of epidermoid carcinoma as it is, namely, single node involvement until late in the course of the disease, it is possible that a more limited type of removal is adequate. A review of our neck dissections for metastatic epithelioma of the lip has shown quite conclusively that a submental and submaxillary dissection gives as good results in the entire series of cases as does complete dissection with, of course, much less physical strain on the patient.

*Suitable Types of Cases.*—The groups of metastatic cervical nodes coming within the range of this combined method of radiation may be enumerated as follows:

1. Adult type of epidermoid carcinomas with perforation of the node capsule and infiltration of surrounding structures.
2. Early involvements of transitional-cell carcinoma.
3. Metastatic nodes, locally operable, but with advanced unfavorable primary growths.
4. Metastatic nodes, locally operable, but in patients of advanced age or in such general physical condition as to render a complete unilateral dissection unduly hazardous.
5. Nodes operable but bilateral.
6. Recurrent nodes.

It will be seen from this that all of those cases falling within our interpretation of cervical-node operability are eliminated. At the other end of the scale, the very advanced cases—either in local bulk of an individual metastatic process or, as more frequently happens, with generalized involvement of nodes—should be eliminated from consideration of treatment by this means. Too much stress cannot be laid on the inadvisability of attempting radical

measures under such circumstances. The moderate degree of growth restraint which might be obtained by external radiation alone will afford to better advantage the small amount of palliative benefit which it is possible to give these unfortunate cases.

Localized masses and, preferably, single nodes, "inoperable" on our basis of appraisal are, of course, most favorable for this form of therapy. The smaller the masses the more favorable they are physically as well as clinically.

*Technical Procedure.*—In considering the technical procedure, it may be well to repeat that external radiation of maximum intensity, that is, of such intensity as to deliver two or more skin erythema doses within the lymph-node-bearing area, is presupposed in all cases. In some few instances, the metastatic nodes are so located that the trochar radon implantation needles



FIG. 4.—Type of immediate closure with drainage below horizontal incision.

may be inserted directly through the skin and into the node. Such insertion is facilitated by simply nicking the skin at one point with a sharp-pointed scalpel and through this the several punctures for gold tube implantation may be made. In general, however, direct exposure of the node under local anæsthesia is decidedly preferable. Practically any metastatic node in the neck can be exposed through an incision a few centimetres in length and extending through the platysma. A very limited amount of dissection after reflecting the platysma is called for—in fact, the least dissection consistent with adequate exposure of the node and immediately adjacent vital structures is preferable. Maintenance of the blood supply to the node and adjacent parts is of very considerable importance when it comes to withstanding the local effects of 6, 8, or 10 skin erythema doses of radiation delivered by this implantation. The exposure not only lends accuracy to the radon implantation but makes possible the avoidance of damage to blood-vessels and nerves lying immedi-

ately adjacent to the mass or which may be pushed into an abnormal and little-expected position by pressure of the growth.

Direct exposure permits of aspiration of the node for diagnosis after the method advanced by Martin and Ellis. Substantiation of the clinical diagnosis by this means is of very considerable importance in some of the cases and in our experiences has not been dangerous. In a considerable percentage of the cases, the metastatic mass shows some degree of central necrosis and if this, at one point or another, approaches the surface, the subsequent course of the case is benefited materially by draining out this necrotic débris at the time of exposure. The entire area is much less liable to undue inflammatory reaction if this is done.

After the emanation tubes have been implanted, the wound is closed care-

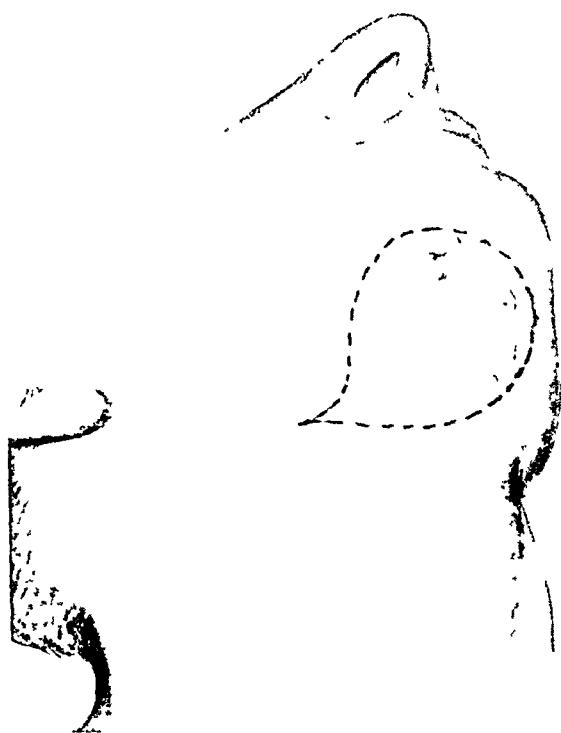


FIG. 5—Recurrent metastatic node showing skin infiltration, central necrosis, and beginning perforation of skin. Dotted line indicates area of skin to be sacrificed.

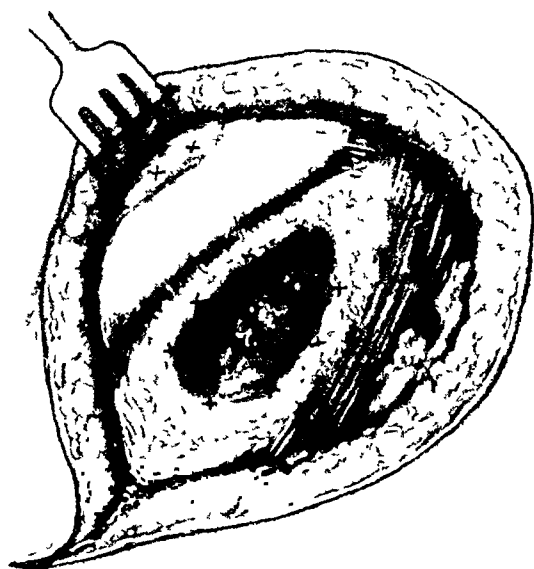


FIG. 6—Deeper portion of mass infiltrates all adjacent structures and along outer surface of mandible. Areas marked x indicate points of gold tube radon implantation. Central necrotic area has been cleaned out

fully, particular care being taken in the approximation of the platysma and of the skin. Provision is made for drainage for the first forty-eight hours following operation. No danger is experienced with healing of the wound from the radiation standpoint if the implantation is properly "timed" with respect to the external irradiation. If the external dosage has been delivered within a brief period—a week—then the exposure and implantation may be carried out at once and primary healing obtained before the maximum skin reaction has been reached. While exposure and implantation are not precluded by an intense local reaction, nevertheless, they are inadvisable if they may be avoided. Unless there is some urgent reason for going ahead with it, we favor waiting until the maximum intensity of external radiation has



been passed. Meticulous care should be given the matter of surgical technic at every turn even though the operative procedure is a very small one. If infection is avoided, there will be no trouble, under ordinary conditions, with wound healing. If primary healing is not obtained, the delay in secondary union incident to the intense radiation leaves a very trying wound to deal with for several weeks—a daily reminder of initial carelessness.

In addition to the routine skin preparation, pre-operative painting with 5 per cent. picric acid solution is preferred to iodine. The latter is too irritating on a skin which has been subjected recently to heavy external irradiation. Immediate post-operative dressings of sterile gauze wrung out of alcohol seem to have some advantages over plain sterile gauze and after the stitches have been removed, on the fourth or fifth day, albolene-soaked gauze aids materially in relieving the skin irritation.

One other factor which calls for particular emphasis, in fact, upon which the efficiency of the entire procedure rests, is the intensity of the radiation thus delivered by direct implantation. Reference should again be made to the dosage intensity calculations of Martin and Quimby wherein the adult types of epidermoid carcinoma require a minimum dosage to all parts of the tumor-bearing area of 7 to 10 skin erythema doses, while the more radiosensitive undifferentiated types require at least 3 to 5 skin erythema doses.

This work of intensity measurements was begun as a study in retrospect and later applied to the calculation of doses to be delivered. Our experience has been that unless these factors are adhered to as minimum standards in selecting the total doses for interstitial implantation, the mass in question will not be completely controlled. This method aims at complete local control of growth, even though it be but for palliative purposes. Unless, therefore, full doses by implantation are employed the principle of the method is obviated. Partial control can be obtained by external radiation alone. Unless one expects to obtain complete control of a given metastatic mass, then interstitial implantation of filtered radon should not be resorted to.

*Hazards of Implantation Technic.*—As with any radiation method, there are certain dangers and hazards attendant upon the interstitial placement of point sources of radon energy of such intensity as those which we ordinarily employ in this procedure—0.3 millimetre gold radon seeds containing 2 millicuries of emanation, or slightly over this amount. We have never experienced the unpleasantness of puncture of large vessels, although it is probable that this would be a very real hazard if blind puncture were done routinely through the skin. Direct exposure of the node avoids this and permits also of placing the emanation tubes a few millimetres at least from the large vessels. With masses infiltrating posteriorly over and about the posterior cervical sensory nerves, care must be taken to keep the emanation tubes several millimetres, if possible, from the nerves in order to avoid a very unpleasant period of pain lasting for several weeks. If this cannot be avoided by this manner of tube placement and the case otherwise warrants it, then section of the posterior sensory roots of the area in question should be done.

Over-radiation of bone, particularly along the lower border of the mandible, is to be avoided if possible and if this is not possible, one must be prepared to remove a segment of devitalized bone later. This does not always follow directly, but is more apt than not and should be at least counted upon.

Intense radiation by implantation in close proximity to the submaxillary salivary gland is apt to produce a degree of inflammation in the salivary gland which may interfere with its normal drainage and produce, for a transient period, a considerable degree of pain. Since the salivary gland is prone to low-grade infection of mouth origin, this possibility must always be reckoned with and at times drainage provided. Complicating low-grade mixed infection must always be reckoned with in interstitial implantation as in dealing with tumor tissue under other circumstances. Avoidance of it by attention to every detail of careful surgical technic cannot be emphasized too strongly. Once a heavily radiated wound becomes infected and primary healing inter-



FIG. 7a and b.—Wound only partially closed in order to permit of direct observation, possibly further radon implantation, and removal of sequestrum. Open wound packed with iodoform gauze and drainage established temporarily below it.

ferred with, it is useless to speculate on where the process will end. In the presence of central necrosis of a sizable metastatic node, danger of continued breaking down, out of proportion to that which might otherwise be expected, is a possibility and under such circumstances a reduction in the total implantation dose, at least to the point of minimum safety as indicated by our dosage measurements, is much the safer course. The same is true in principle with fixation and infiltration of skin over the involved node. Unless the questionable area of skin can be sacrificed in making an exposure of the deeper mass, it is doubtful whether such skin will withstand the maximum dosage which we would advocate otherwise.

#### SUMMARY

Complete control of epidermoid carcinoma, metastatic in the neck, is but rarely effected by external radiation alone. Growth restraint only is the expectancy.

Interstitial implantation of filtered radon is offered as a means of supplementing external radiation in the control of localized metastatic cervical nodes of epidermoid carcinoma—nodes inoperable for one reason or another, as stated, yet not in all instances technically inoperable. This method, while essentially local in character, permits of adequate quantitative radiation of a metastatic cervical mass unless it be of unusual proportions.

The procedure offers a reasonable chance, we believe, for complete control of growth in a certain number of metastatic nodes outside the group ordinarily adjudged as surgically operable. It offers a maximum degree of palliative control in a large group of the more advanced cases with a minimum of "damage"—either constitutional or to normal tissues immediately adjacent to the tumor-bearing area.

In view of the fact that a localized metastatic mass may be completely controlled by this method of irradiation, operative surgery is relieved of the necessity for attempting extensive operative procedures in cases where the expectancy from such measures is very little indeed. In some, at least, of the metastatic necks which may reasonably be classed as surgically operable, the method has made so far a very favorable impression and may, with added experience, afford a substitute for complete unilateral dissection.

The importance of avoiding deliberate breaking down of tissue by overdosage of radon seeds is stressed particularly because, once it has occurred, especially in the anterior triangle of the neck, the danger of hæmorrhage from the wound, apart from the several other unhappy possibilities, is very considerable. With but few exceptions, the best interests of the patient are served by maintenance of an intact skin covering.

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# EFFECT OF IRRADIATION UPON A MALIGNANT THYMIC TUMOR

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FROM THE SURGICAL SERVICE OF THE MEMORIAL HOSPITAL

ALTHOUGH there is an extensive literature dealing with tumors of the thymus, it is concerned mostly with the pathology and symptoms. Comparatively meagre reports are available of the treatment of choice of such tumors, namely irradiation, and particularly lacking are reports that include autopsy findings in patients that have been treated by irradiation.

The case here presented, believed to be one of thymic carcinoma, was closely followed for two years and two months. An unusually large amount of radiation was employed. Autopsy showed a practically complete disappearance of the tumor from the primary site and from the adjacent regions to which it had extended, evidently a direct result of the heavy irradiation of these areas.

CASE.—S. B. (Hospital No. 39159), a single woman of thirty-nine years, came to the Memorial Hospital January 23, 1928, complaining chiefly of cough and dyspnoea. She stated that she had become ill about one year before. At that time she had suddenly begun to vomit and had noticed a trace of blood in the vomitus. Soon afterward she began to cough, and during the year the cough had become more troublesome and was accompanied by considerable sputum. She had not observed any blood in the sputum. The vomiting had not recurred, but her appetite had become very poor. She had become moderately constipated, but had seen no blood in her stools. She had lost twenty pounds.

For four months she had noticed in her breasts a variable degree of induration, accompanied by the presence of lumps which seemed to disappear from time to time. For six weeks she had had a good deal of difficulty in breathing.

Her family history was negative. Her past history was negative, with the exception of an operation which had been done five years previously for "replacement of a displaced tube," and removal of the appendix. She had had two uterine hæmorrhages, each lasting a week, before this operation.

Upon her admission to the clinic, January 23, 1928, she appeared poorly nourished. The eyes, ears, nose, teeth and oral mucous membranes were negative. In the oropharynx a slight dilatation of veins could be seen.

There was a marked swelling of the superficial veins over the anterior chest wall, extending to the supraclavicular spaces and the neck, and to the upper part of the abdomen. The thyroid gland did not seem enlarged, but the trachea was slightly displaced to the left. The examination of the heart seemed negative. There was a marked increase in the width of the mediastinal dulness anteriorly, and in the degree of dulness. At the base of the right lung anteriorly, a pleural friction rub was heard; while at the base of the left lung the signs seemed to indicate the presence of a small amount of fluid.

In the abdomen, in addition to the engorgement of the veins of the upper half, there was in the right upper quadrant a feeling of fulness and resistance to palpation, suggesting an enlargement of the liver, although the liver's edge could not be felt.

Pelvic examination was negative.

The blood count gave practically normal findings, as follows: Hæmoglobin 80 per cent., red blood corpuscles 4,480,000; white blood cells 8,800; polymorphonuclear cells 70 per cent.; large lymphocytes 6 per cent.; small lymphocytes 16 per cent.; transitional cells 4 per cent., eosinophile cells 4 per cent.

The röntgenogram of the chest (Fig. 1) showed a large, centrally located mediastinal mass, together with some thickened pleura and fluid at both bases.

A provisional clinical diagnosis was made of either thymoma or mediastinal lymphosarcoma.

*Treatment.*—The patient's chest was irradiated by means of high-voltage Röntgen-rays, the radium emanation and radium packs as follows:



FIG. 1.—On admission January 23, 1928; showing large mediastinal mass.



FIG. 2.—A little over four months after admission, showing marked regression of mediastinal mass. There is evidence of thickened pleura and fluid at both bases

#### *High-Voltage Rontgen Rays*

| Date    | Area                         | Time<br>(min.) | Kilovolts<br>(peak) | Milli-<br>amperes | Distance<br>(cm.) | Filter                 |
|---------|------------------------------|----------------|---------------------|-------------------|-------------------|------------------------|
| 1/26/28 | Right chest anteriorly.. .   | 10             | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |
| 1/28/28 | Right chest posteriorly ..   | 10             | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |
| 1/31/28 | Left chest posteriorly... .. | 10             | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |
| 2/ 3/28 | Left chest anteriorly. ...   | 10             | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |
| 2/ 6/28 | Right chest laterally... ..  | 10             | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |
| 2/ 8/28 | Left chest laterally.....    | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 6/23/28 | Mediastinum anteriorly       | 7              | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |
| 6/28/28 | Mediastinum posteriorly.     | 7              | 185                 | 30                | 50                | 0 5 mm. Cu<br>3 mm. Al |

# MALIGNANT THYMIC TUMOR

| Date    | Area                            | Time<br>(min.) | Kilovolts<br>(peak) | Milli-<br>amperes | Distance<br>(cm.) | Filter                 |
|---------|---------------------------------|----------------|---------------------|-------------------|-------------------|------------------------|
| 7/ 2/28 | Mediastinum anteriorly . . . .  | 7              | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 7/ 5/28 | Mediastinum posteriorly . . . . | 7              | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |

## *Radium Emanation Pack*

| Date    | Area                             | Millicurie<br>hours | Distance<br>(cm.) | Filter      |
|---------|----------------------------------|---------------------|-------------------|-------------|
| 9/19/28 | Mediastinum anteriorly . . . . . | 10,000              | 10                | 2 mm. brass |
| 9/20/28 | Mediastinum anteriorly . . . . . | 10,000              | 10                | 2 mm. brass |

## *High-Voltage Röntgen Rays*

| Date     | Area  | Time<br>(min.) | Kilovolts<br>(peak) | Milli-<br>amperes | Distance<br>(cm.) | Filter                 |
|----------|---|----------------|---------------------|-------------------|-------------------|------------------------|
| 12/15/28 | Right lower chest anteriorly  | 4.5            | 175                 | 30                | 30                | 0.5 mm. Cu<br>3 mm. Al |
| 12/19/28 | Right lower chest posteriorly   | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 3/ 9/29  | Right lower chest anteriorly,<br>including lower mediasti-<br>num           | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 4/12/29  | Right supraclavicular, di-<br>rected toward mediastinum                     | 11             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 4/26/29  | Left supraclavicular, directed<br>toward mediastinum                        | 11             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 5/ 7/29  | Mediastinum anteriorly,<br>lower one-half                                   | 10             | 175                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 5/10/29  | Right lower chest, antero-<br>laterally                                     | 10             | 175                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 7/29/29  | Right chest anteriorly, mid-<br>dle third, obliquely toward<br>mediastinum  | 10             | 175                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 8/ 2/29  | Right chest posteriorly, mid-<br>dle third, obliquely toward<br>mediastinum | 10             | 175                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 8/ 6/29  | Left chest posteriorly, mid-<br>dle third, obliquely toward<br>mediastinum  | 10             | 175                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 8/ 9/29  | Left chest anteriorly, mid-<br>dle third, obliquely toward<br>mediastinum   | 10             | 175                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 10/22/29 | Mediastinum anteriorly . . . .  | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 10/25/29 | Right lower chest anteriorly  | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 10/29/29 | Right lower chest posteriorly   | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 11/23/29 | Right lower chest laterally . .   | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |
| 11/27/29 | Left supraclavicular space . .  | 10             | 185                 | 30                | 50                | 0.5 mm. Cu<br>3 mm. Al |

# LLOYD F. CRAVER

## *Radium Pack*

| Date    | Area                        | Milligram<br>hours | Distance<br>(cm.) | Filter                        |
|---------|-----------------------------|--------------------|-------------------|-------------------------------|
| 1/31/30 | Right chest anteriorly..... | 8,000              | 10                | 0.35 mm. Pb<br>1.50 mm. brass |
| 2/ 1/30 | Right chest anteriorly..... | 4,000              | 10                | 0.35 mm. Pb<br>1.50 mm. brass |
| 2/ 2/30 | Right chest laterally.....  | 7,000              | 10                | 0.35 mm. Pb<br>1.50 mm. brass |
| 2/ 3/30 | Right chest posteriorly.... | 4,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/ 4/30 | Right chest anteriorly..... | 7,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/ 5/30 | Right chest anteriorly..... | 1,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/ 5/30 | Right chest laterally.....  | 7,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/ 7/30 | Right chest posteriorly.... | 8,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/ 8/30 | Right chest laterally.....  | 1,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/ 8/30 | Right chest anteriorly..... | 5,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/10/30 | Right chest laterally.....  | 8,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/13/30 | Right chest posteriorly.... | 6,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/14/30 | Right chest laterally.....  | 2,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |
| 2/14/30 | Right chest posteriorly.... | 5,000              | 10                | 0.35 mm. Pb<br>1.5 mm. brass  |

*Course.*—Within a month following the first series of röntgen treatments, a marked regression of the mediastinal mass took place, accompanied by a marked decrease of all symptoms and a gain in weight. The dyspnœa disappeared and there was very little cough. The dulness over the mediastinum decreased considerably in extent, but over the lower half of the sternum the percussion note remained definitely flat. The röntgenogram (Fig. 2) still indicated some thickening of the pleura and the presence of fluid at both bases.

Three months later, in June, 1928, the dilatation of the veins over the chest wall and neck had disappeared.

The second series of treatments given during June and July, 1928, was not followed by further improvement. In fact, the cough recurred, and in August, 1928, the film of the chest indicated some extension of the mass into the right lung. At this time the blood count showed moderate anæmia and some leucopenia, possibly the result of the irradiation. Clinically it was soon found that the mediastinal dulness was more marked, and that above the left clavicle there was a definite mass of moderately enlarged, firm, discrete nodes.

Because of these findings, further irradiation was indicated. This time, September 19 and 20, 1928, the radium emanation pack was used because the second cycle of Röntgen-rays had failed to give relief and it was hoped that the tumor would respond better to radium. While some relief did follow the use of the emanation pack over the mediastinum anteriorly it was of short duration. \* Dyspnœa and cough soon became troublesome again.

In November, 1928, examination of the chest showed marked decrease of breath sounds over a zone about 10 centimetres in width around the front and side of the right lung at the base, continuous with the area of dulness over the lower half of the sternum. From that time this area of decreased breath sounds persisted practically unchanged. Over this region the percussion note later became dull and this sign also persisted. These findings corresponded with a gradual extension into the right lung as shown by röntgenograms.

During 1929, the patient's condition seemed to change but little. Pain, cough and dyspnoea, while persisting to a moderate degree, did not prevent the patient from continuing to work daily as a stenographer. In April 1929, an enlarged node in the inner part of the right supraclavicular fossa was found. It regressed almost completely following treatment with high-voltage Röntgen-rays. Altogether during 1929 fourteen röntgen treatments were given, mostly about the right lower chest and mediastinum. The patient bore these treatments well. She suffered comparatively little radiation sickness and usually had some symptomatic relief, which was, however, only temporary.

In January, 1930, her symptoms all increased to such a degree that she was compelled to give up work and take to bed. At this time she began to have considerable hæmoptysis. The nodes in the inner part of each supraclavicular space again became enlarged and firm, and for the first time a definitely involved node was found in the right axilla, 1.5 centimetre in diameter. The prognosis seemed hopeless for any further palliation, considering the amount of radiation that had already been used. Moreover the exquisite tenderness of the lowermost ribs in the right side, in the area which had been so heavily irradiated, raised a question of radiation osteitis. However, the severity of her symptoms demanded another attempt at palliation. Accordingly she was admitted to the hospital. This time, January 31 to February 14, 1930, the radium element pack was used over the right chest, over various areas, mostly directed toward the mediastinum. A total of 73,000 milligram hours at 10 centimetres was given. During the course of treatment definite improvement could be seen. The hæmoptysis practically ceased and both pain and dyspnoea lessened considerably. The tenderness of the ribs, however, persisted, but later diminished somewhat following the patient's return to her home.

The enlarged nodes in the supraclavicular spaces and in the right axilla almost disappeared, and some definite clearing of the shadow in the right lung was found on the röntgen film but the dulness and diminished breath sounds previously noted over the lower mediastinum anteriorly and over the right lower chest persisted. In addition a few sonorous râles were heard (March 10, 1930) over the base of the left lung posteriorly.

About March 20, 1930, following the exertion of taking a bath, there was a rather sudden increase of pain and dyspnoea and two days later, March 22, 1930, she died.

*Autopsy.*—(Done by Dr. F. W. Stewart forty-eight hours after death.) The body, which had been embalmed, was that of a well-developed and well-nourished adult female. There was moderately excessive development of hair in the axillæ and on the upper lip. The pubic hair showed normal distribution. No œdema was seen. No superficial lymph-nodes were palpable. Both breasts were lumpy, and on section showed a diffuse fibrous and cystic mastitis with large cysts, some containing thick fluid. The skin over the right chest wall anteriorly was deeply bronzed.

*Thorax.*—Both pleuræ were adherent. The tissues in the region of the thymus and the anterior pericardium were thickened and fibrotic, but no gross tumor could be found. The left lung was separated from the chest wall with difficulty. Its pleura was thickened. Its lower lobe appeared to show a partial diffuse consolidation, somewhat obscured by the changes resulting from the embalming. At the base of the left lung toward the periphery was a small semi-necrotic tumor nodule. In the right lung anteriorly was a large empty cavity (Fig. 3) 8 by 6 by 6 centimetres. Its long axis lay longitudinally.



It extended from near the mediastinum almost to the lateral chest wall. Its walls were hard, fibrous and trabeculated, and contained a very few small nodules, apparently residual tumor tissue. A few trabeculae containing blood-vessels crossed the cavity. The bronchial nodes were large and one contained a semi-necrotic tumor nodule. The bronchi contained faintly yellowish mucus.

The heart was normal. The spleen was slightly enlarged; its markings could not be seen clearly because of the changes caused by embalming. The liver and pancreas seemed normal. The right adrenal contained a small diffuse metastasis to the medulla. The left adrenal was cystic in the centre. The gastro-intestinal tract seemed normal. The lymph-nodes about the coeliac axis were enlarged and hard and showed foci of



FIG 3 —Large cavity in right lung

necrosis. The kidneys were negative. The ovaries were fibrosed and atrophied. The bladder and uterus seemed negative externally and were not sectioned.

*Anatomical Diagnosis.*—Mal'ignant tumor of undetermined origin; probably thymoma. Metastases to lungs, bronchial and aortic abdominal lymph-nodes and to right adrenal. Pneumonia, fibrous pleuritis, fibrosis of thymic and anterior pericardial regions, atrophy of ovaries, chronic cystic mastitis, enlargement of spleen.

*Microscopic Diagnosis.*—(Fig. 4.) Doctor James Ewing's report was as follows: "The structure of the tumor is best preserved in the abdominal lymph nodes, where the effects of radiation were less pronounced. Here the sections show a highly malignant tumor process, presenting large round and polyhedral cells, with large hyperchromatic nuclei. There are occasional very large giant cells. Mitotic figures are rather numerous. Many of the areas show many lymphocytes, and here the process suggests a granuloma

## MALIGNANT THYMIC TUMOR

with sarcomatous changes. In most areas the tumor tissue is composed exclusively of large polyhedral or round cells, and here the process resembles carcinoma. The diagnosis seems to be a primary malignant tumor of the thymus arising from the reticulum cells. Since these cells are of epithelial derivation the tumor may be called a thymic carcinoma, but since there are many lymphocytes accompanying the process, it is possible that the disease began as a thymic granuloma, which assumed more malignant properties in its later course."

### SUMMARY

A case is presented originally having definite evidence of a large mediastinal mass believed to be a malignant thymic tumor, probably car-

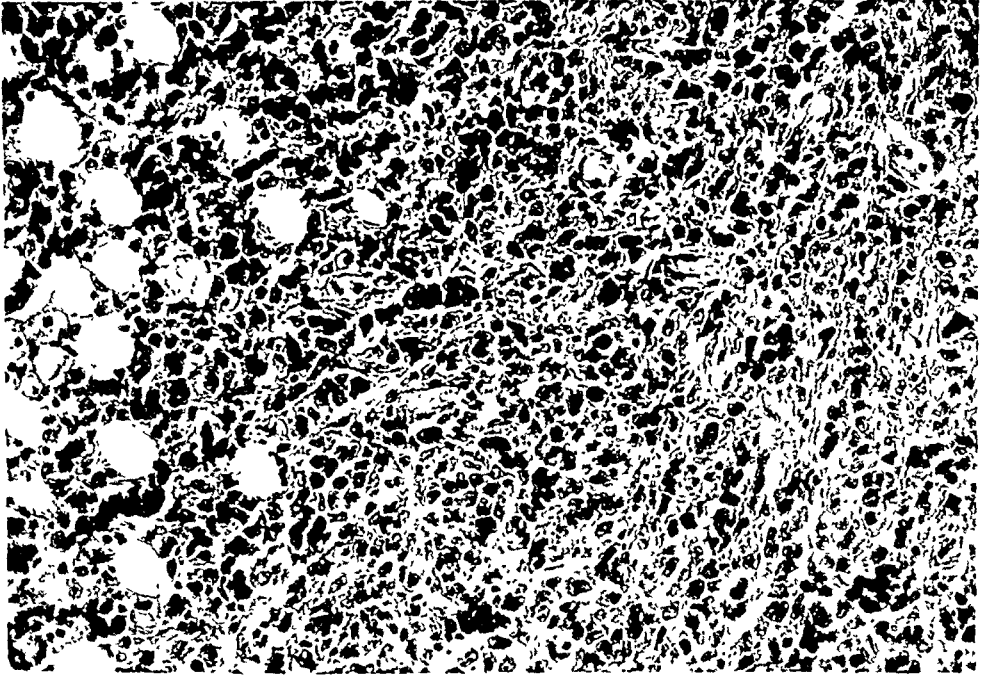


FIG. 4.—Microphotograph of section from an abdominal node.

cinoma, in which treatment resulted in the complete disappearance of all evidence of tumor at the primary site, and in which at autopsy a large cavity with healed walls was found in the right lung anteriorly near the mediastinum. It is believed that this cavity had been the seat of tumor tissue which disappeared as a result of the heavy irradiation with both radium and Röntgen-rays. Various small scattered metastases were found in the bronchial lymph-nodes, the left lung, the right adrenal gland and the aortic abdominal nodes, of which all except the bronchial nodes lay outside of the area that was irradiated.

## RESULTS IN THE RÖNTGEN-RAY THERAPY OF GIANT-CELL TUMORS OF BONE

BY RALPH E. HERENDEEN, M.D.

OF NEW YORK CITY

AT A meeting of the Eastern Section of the American Röntgen-ray Society in January, 1924, the writer read a paper dealing with the effects of Röntgen rays on giant-cell tumors of bone. This article recorded, for the first time, some observations indicating that not only could a majority of them be cured, but in many instances this method was superior to the standard surgical methods of treatment.

It has been suggested that this work be reviewed with the object of comparing the statements made at that time, now more than six years ago, with the information available to date on the present status of those cases.

The majority of the patients studied in presenting that report had been under treatment and observation for three or four years. Several had gone one or two years, and a few about five years, so that a report at this time on the status of those cases, all of which have now gone more than five years since the first treatment, should be of interest in determining the value of X-ray therapy in giant-cell tumors of bone.

The tumors studied which formed the basis for that report were of great variety and location, and although most of them were undoubtedly true benign giant-cell tumors, it may be that in some instances the biopsy findings, along with the clinical history, physical and röntgenographic findings, and course of the disease after treatment, justify a diagnosis of GIANT-CELL SARCOMA, or MALIGNANT GIANT-CELL TUMOR, an expression used lately in some of the reports coming from the Pathological Laboratory of the Memorial Hospital.

The term "giant-cell sarcoma," which was left out of the classification of bone tumors adopted by the Committee of the College of Surgeons for the Registry of Bone Tumors, might have been left in, without seriously impairing the value of this new classification or terminology for bone tumors.

It might be well at this point to state that at times there does appear to be a tumor which possesses some of the röntgenographic and histological features of benign giant-cell tumors, but potentially malignant as shown by subsequent developments.

Stone and Ewing report the occurrence of a giant-cell tumor in the head of a tibia in a male aged nineteen, which, later after curettage, recurrence, and subsequent ineffectual attempts to control the disease, became transformed into a malignant, metastasizing tumor, which caused the death of the patient in spite of an amputation performed before there was any evidence of metastasis to the lungs.

It is believed that a larger percentage of giant-cell tumors recur after curettage than is commonly supposed. From our experience at the Memorial Hospital it is estimated that about 25 per cent. of all giant-cell tumors recur after curettage. Out of this number a large percentage are giant-cell tumors of the head of the tibia, and in most instances where a malignant transformation developed subsequently, the tumor occurred in the head of a tibia. Just why such an unduly large number of these cases occur in this location has not been explained. It appears, therefore, that the surgical treatment of giant-cell tumors in this location should be altered from the standard procedure of simple curettage and swabbing out of the cavity with carbolic acid or zinc chloride. Adequate pre-operative radiation and the use of a heavy bone transplant might lead to fewer recurrences here and more prompt callus production.

There probably is no other single factor of greater clinical significance in the differential diagnosis of giant-cell tumors than the location. Codman states that one of the requisite factors in diagnosing giant-cell tumors of the long bones is the presence of the tumor in the end of the bone or epiphysis, and not in the diaphysis or shaft. The tumor, he states, must be in, or extend into the epiphysis, or well into the end of the bone. This dictum is not accepted by all observers, and should be qualified when an epiphyseal line is present and the tumor may be in the shaft. An example is demonstrated in Case III.

In those instances where the tumor occurs in an unusual location, regardless of the fact that the history and radiographs are characteristic, it seems wise to exercise considerable care before the tumor is definitely classified as a benign giant-cell tumor.

It seems that mechanical pressure determines to some extent the amount of growth restraint and the degree of malignancy. Tumors that are firmly encapsulated or surrounded by dense, unyielding structures may remain relatively benign from a clinical standpoint for a long time though potentially malignant from a histological viewpoint. In this respect, the location of a giant-cell tumor is an important consideration in the prognosis and treatment.

Case I illustrates some of the above points: This case was so characteristic of a giant-cell tumor from the röntgenographic standpoint that Kolodny cites it as a typical example, but it will be noted that the location is an unusual one for a giant-cell tumor. Two years after this patient's first visit to the Memorial Hospital, and approximately a year after the film was obtained which was shown by Kolodny in his article, another tumor, apparently metastatic from the primary growth in the distal end of the humerus, developed in the ascending ramus of the right inferior maxilla. Although multiple giant-cell tumors do not occur, the appearance of this growth two years after the first tumor appeared in the humerus, makes this conclusion hardly tenable.

Furthermore, the character and location of the subsequent growths strongly indicate that the primary tumor, if a giant-cell tumor, deserves the diagnosis of giant-cell sarcoma.

RALPH E. HERENDEEN

CASE I.—Woman, aged sixty-five years, was admitted to the Memorial Hospital in October, 1924. She stated that about six months previously she began having pain in



FIG. 1.—Case I. Before röntgen therapy.



FIG. 2.—Case I. After röntgen therapy.

the right arm and elbow. No history of an injury was elicited. The pain here was followed by swelling which increased rather rapidly. The pain increased in severity and the entire elbow and lower one-half of the humerus, including the forearm and hand.

finally became markedly swollen and tender. During this period she was treated by her family physician for rheumatism and neuritis. As it became apparent, however, that



FIG. 3.—Case I. Five year result.



FIG. 4.—Case I. Showing destruction in ascending ramus.

the patient was not improving, she was referred to Doctor Ewing who referred her to the Memorial Hospital.

A film made here on her first visit (Fig. 1) showed a destructive process involving the lower end of the humerus. It appeared to be medullary in origin but of rather rapid growth, dilating the medullary portion of the bone, infiltrating the cortex, and extending out about it into the surrounding soft parts. The tumor responded readily to Röntgen-ray therapy. The pain diminished rapidly, the swelling subsided in the hand, forearm, and arm, then more slowly at the elbow. Films made from time to time reveal (Figs. 2 and 3) definite evidence of bone regeneration. Tenderness and pain finally disappeared and the patient was able to use her hand, wrist, and her elbow to a certain extent. Later on the function at the elbow improved to such an extent that limitation in motion was perhaps only 30 per cent. of normal. This condition continued for about two years when suddenly the patient began experiencing pain in the right side of the face. This was accompanied by tenderness and swelling over the ascending ramus of the right inferior maxilla. A film (Fig. 4) was obtained which showed a large, clean-cut area of bone destruction in the mid-portion of the ascending ramus. A moderately heavy dose of Röntgen-rays was applied here with a very prompt response.

The pain and swelling promptly disappeared and there has been no recurrence here or in the elbow, but subsequent to the appearance of this second tumor, during the past four years, others have appeared approximately from four to eight months apart. One appeared in the right occipital region, another in the sternum, another in the upper end of the left humerus, one in the lower end of the right tibia, and recently, the last to appear, over the sternal end of the right clavicle, and each of these tumors on treatment disappeared promptly and did not recur.

Each of the subsequent tumors developed in a new site. Except for the short periods during the development and treatment of the tumors the patient has been well, up and around, and able to attend to a certain amount of her household duties.

The case is reported (1) because it illustrates an unusual type of giant-cell tumor which we believe should be classified as giant-cell sarcoma or malignant giant-cell tumor, and (2) the palliative value of Röntgen therapy.

That a considerable percentage of error in Röntgen-ray diagnosis of giant-cell tumors occurs is not denied, but routine biopsy to establish the diagnosis, when the clinical history, physical and röntgenographic findings are characteristic, is not only unnecessary, but may lead to infection, dissemination of tumor cells, acceleration of the growth by breaking down the mechanical barrier about it; and furthermore, it not uncommonly happens that when a positive diagnosis is difficult without a section, the report of microscopical findings is as uncertain as the röntgenographic. Also if Röntgen therapy is subsequently employed, the repair process may be hindered and delayed, more deformity may result, and the end-result may not be so satisfactory as if no incision had been made.

The most common sites for benign giant-cell tumors of the bones are found in the ends of the bones, at the knee-joints, and at the distal ends of the radii; but we have seen them in the skull, spine, ribs, pelvis and os calcis, as well as in either end of all of the long bones of the extremities.

The typical röntgenographic features of giant-cell tumors are usually so characteristic as to need little comment. An excellent example is to be found in Case II (Figs. 5, 6 and 7).

CASE II.—Man, aged twenty-eight years, first began to experience pain in the left knee, especially after walking. This persisted and gradually became worse so that the patient was unable to walk without a limp. About July, 1922, he was given ultraviolet

# X-RAY THERAPY GIANT-CELL TUMORS OF BONE

FIG. 5.—Case II. Before Röntgen therapy.

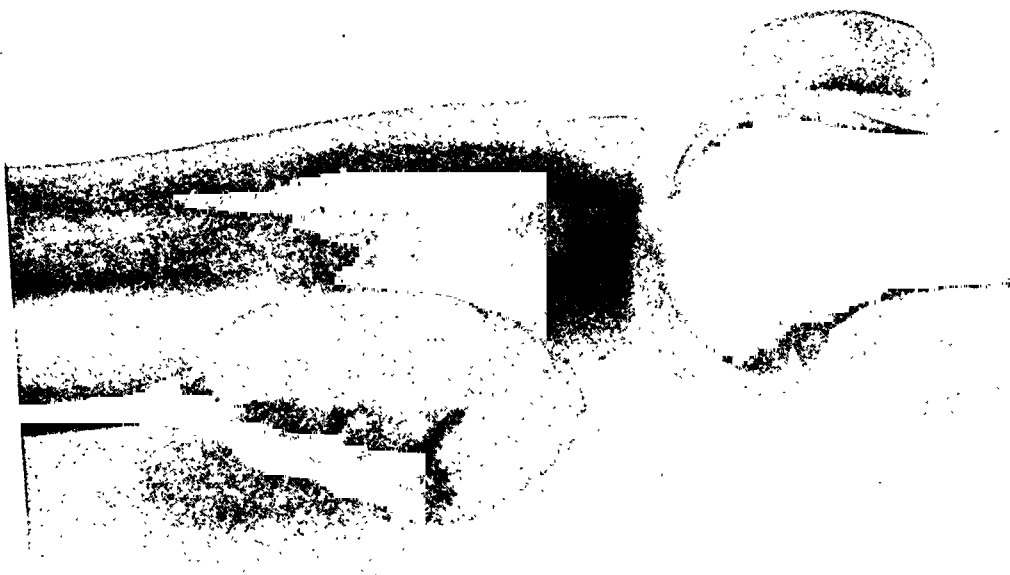


FIG. 6.—Case II. During röntgen therapy.



FIG. 7.—Case II. Seven years after treatment.





ray treatment by his physician who thought the condition was rheumatic. Later the patient noticed a swelling at the site of the pain. This increased in size, and the pain persisted. The patient was finally referred to the Memorial Hospital where he reported in March, 1923. The films reveal classical features of a giant-cell tumor. The first Röntgen-ray treatments were followed by some reaction as the dose was fairly heavy. The pain and aching diminished and the tumor became firm on palpation. Films made later on reveal evidence of beginning ossification.

At the present time the tumor is entirely healed, bony hard. The patient has no symptoms, walks without a limp, and there is no impairment in function of the knee. This is a seven-year cure.



FIG 8.—Case III. Before Röntgen-ray treatment. (Anterior view.)



FIG 9—Case III. Before Röntgen ray treatment. (Lateral view.)



FIG 10—Case III Three months after last X ray treatment (Lateral view.)

The tumor occurs in an end of a long bone. It is medullary in origin and symmetrical in growth, dilating equally in all directions the medullary portion of the bone, and thinning out the cortex. A characteristic trabeculated appearance is present. The tumor does not extend for any distance through the medullary cavity, and does not extend along the cortex destroying it, and does not infiltrate the soft parts, producing bony growth as noted in osteogenic sarcomas or endothelial myelomas.

CASE III.—Boy, aged eleven years, referred in July, 1925, from the Brooklyn Hospital, with the history that in November, 1923, he sprained the left wrist. Two months later he again injured the left forearm. Two months later the wrist began to pain and

## X-RAY THERAPY GIANT-CELL TUMORS OF BONE

a swelling was noted over the lower end of the radius. A physician was consulted who treated it with massage and put the forearm in a splint for three weeks. In April, 1924, a biopsy was done and soon afterward an operation was performed which consisted of curettage, cauterization and insertion of a substantial bone transplant. Three months later the wrist began to pain and later an enlargement was noted. This persisted off and on for several months, then began to increase. The patient consulted a physician at the Brooklyn Hospital and from there he was referred to the Memorial Hospital for Röntgen-ray treatment.

The examination here disclosed a tumor mass in the lower third of the left forearm



FIG. 11.—Case IV. Before Röntgen therapy.



FIG. 12.—Case IV. Five years after Röntgen therapy.

about three times the size of the opposite or normal wrist. The Röntgen-ray films obtained reveal the location, size, and extent of the recurrence. They also show that the bone graft has been completely destroyed. Röntgen-ray therapy was started and only four treatments were given—two in October and two in December. Each exposure was a suberythema dose. No reaction was obtained and instead there was a continual decrease in the size of the tumor which, by the first of January, 1925, or three months after the patient's first visit here, was so marked that it was decided to discontinue treatments, keep the patient under observation, and obtain films from time to time. These demonstrate the effect of radiation and the effort at bone regeneration.

This case demonstrates several of the statements made above: First, that giant-cell tumors occur in the shaft when an epiphyseal line is present, and not in the epiphysis as stated by Codman, but perhaps of greater importance is the demonstration of superiority of radiation over surgery in the treatment of giant-cell tumors located here. Those who have seen the surgical results of treatment of giant-cell tumors here in the lower end of the radius are impressed first by the large number of recurrent tumors after curettage, and secondly, by the marked deformity resulting from subsequent curettements and by the large number of cases which finally require resection and bone transplant. In many instances, although the patient is cured of the tumor, a marked deformity of the wrist-joint results and the function of the

wrist and hand markedly impaired. It is felt that although failures in the Röntgen therapy of the giant-cell tumors in this location have been reported, these cases should all be treated by Röntgen-ray therapy first before an operation is resorted to. The only recurrence of a giant-cell tumor after radiation in our series of cases was a tumor which occurred in the lower end of the radius. The recurrence, however, was treated successfully, and the patient has now gone five years since the recurrence was treated, with no evidence of the disease at the present time, and a good functional result at the wrist (Figs. 7, 8 and 9).

CASE IV.—Boy, aged five years, admitted to the Memorial Hospital from the New York Orthopedic Dispensary and Hospital in November, 1924 with the history that about two and one-half years previously he was seized with pain in the left heel. Some swelling was noted and the foot and ankle were put in a plaster case for three months. The condition continued to get worse, and the leg was then put into a brace. This, however, did not improve conditions and the patient was referred here where X-ray films were made. These revealed extensive destruction of the os calcis. The heel had so enlarged that it was approximately the size of a large orange, extremely tender, the skin tight and reddened. The patient could not walk. The destruction was so extensive that it was difficult to feel sure as to the nature of the process. It was believed that even though the tumor were of a benign nature, or a giant-cell tumor, if Röntgen therapy succeeded in controlling the growth the deformity of the foot would be so great that it would probably be useless as a weight-bearing structure.

The patient's mother was advised to submit the child to an amputation. This she refused to do and insisted that Röntgen therapy be tried. The response to the first two treatments was prompt and satisfactory. There was first relief from pain; next, a progressive but slow diminution in size of the tumor was noted; it became firm to touch and the tenderness disappeared. (Figs. 11 and 12.) At the present time the patient walks without any difficulty. He is able to stamp his foot down on the pavement without pain and it is believed that by the time he reaches manhood, through the normal growth of the foot, the comparative deformity will be very little. This is a six-year cure.

CASE V.—Man, aged twenty-two years, came to the Memorial Hospital in May, 1920. In July, 1918 he fell and twisted his leg which caused a great deal of pain in the left hip. He was not able to be up and about for a week. Since that time he has had several similar injuries, all of which, although some of them have been slight, caused a great deal of pain and some disability. The aching finally became fairly constant, and was especially severe after hard work, heavy exercise, and walking. It was impossible for him to sit long with comfort, and he was unable to sleep on his left side. Finally he noticed definite enlargement of the left hip.

Examination revealed a rather smooth, regular enlargement of the ramus of the left ischium, and on rectal palpation a definite bulging through into the pelvis was palpated. The films of the pelvis made on his first visit reveal evidence of a diffuse destructive process, apparently medullary in origin, involving the ischium and extending up into the ilium back of the acetabulum, where it bulged through into the pelvis. A faint line is noted here, indicating its extent in this direction.

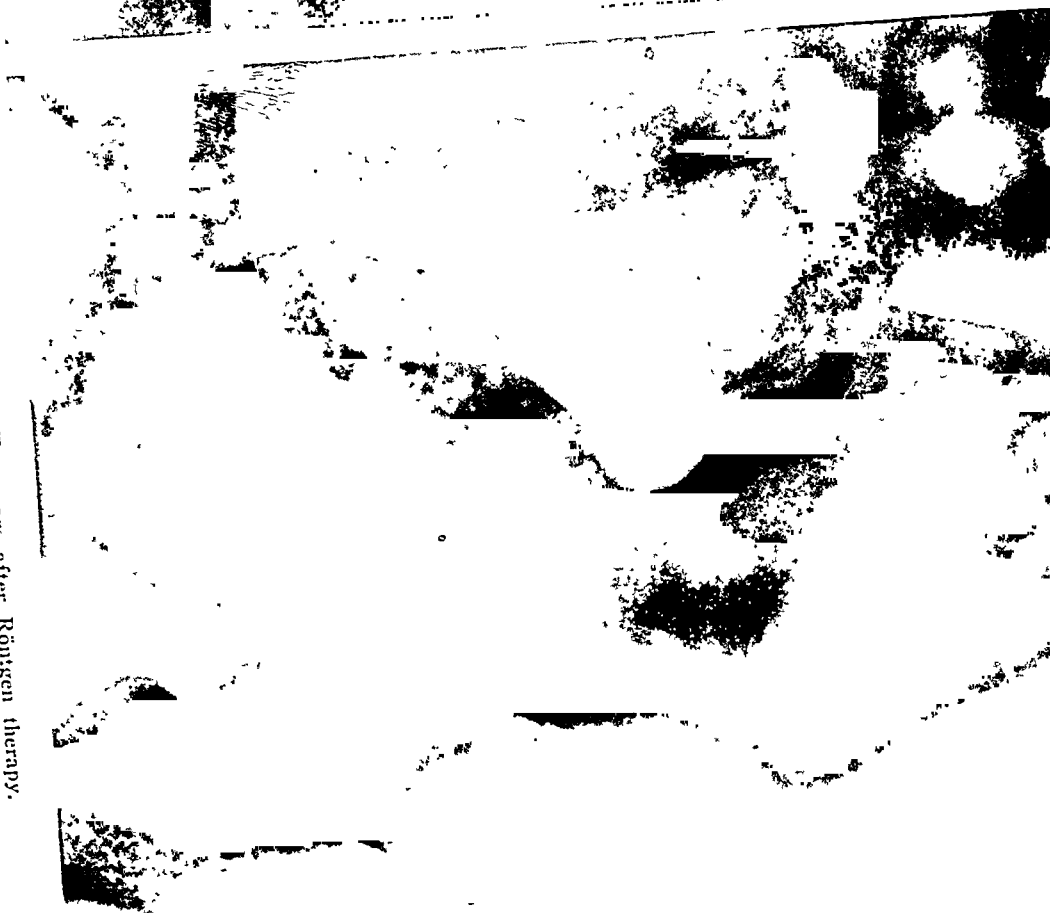
Although this tumor was classified as a giant-cell tumor, the film shows a destructive ability not ordinarily possessed by the benign giant-cell tumors. If this tumor were located in the shaft of a long bone it would probably be classified as an endothelial myeloma or a Ewing's tumor.

The first two Röntgen-ray treatments were followed by a gradual relief from pain. The swelling slowly subsided, and the subsequent films showed a beginning and a progressive effort at bone regeneration. The patient was able to return to his occupation

FIG. 13.—Case V. Before Röntgen therapy.



FIG. 14.—Case V. Ten years after Röntgen therapy.



within six months, and has continued at work since that time. He has no limp and no limitation in motion at the hip-joint. The films show that the tumor has become densely ossified. This is a ten-year cure and demonstrates the usefulness of Röntgen therapy in inoperable bone tumors, inoperable from the standpoint of location and extent (Figs 13 and 14).

CASE VI—Man, aged thirty-seven years, was referred to the Memorial Hospital March 27, 1924, from the Mary Immaculate Hospital in Jamaica, New York, with the history that in July, 1920, he fell and struck the right knee. He was off duty for three weeks. Two to three years later he again injured the knee and was off two weeks. In

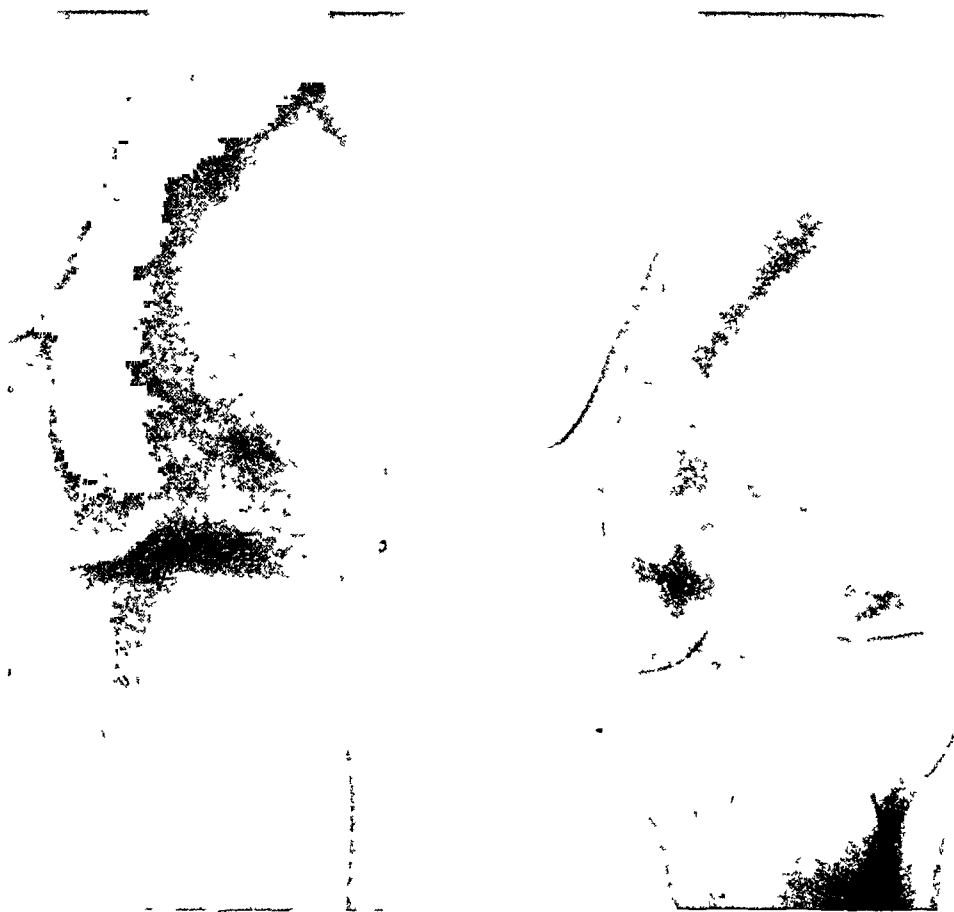


FIG 15—Case VI Before Röntgen therapy. FIG 16—Case VI After Röntgen therapy (Anterior view)

February, 1924, he wrenched the knee while working and since that time has been unable to return to duty. At the Memorial Hospital films which were made revealed a destructive process in the lower end of the femur (Fig. 15). It extends down to the joint surface of the condyles, is approximately the size of an orange, and only a small portion of normal bone remains in the distal end of the femur along the inner side of the cortex above the inner condyle.

Röntgen-ray therapy was followed by relief from pain; the soft-parts swelling slowly subsided; the tumor became firm on palpation and the X-ray films made later (Fig. 16) from time to time demonstrate a continuous effort at bone regeneration.

This case illustrates the results obtainable in the treatment of giant-cell tumors of the lower end of the femur. It is a six-year cure. Attention should be directed especially to the function of the knee-joint. It will be seen that the joint space is normal in width

## X-RAY THERAPY GIANT-CELL TUMORS OF BONE

and contour and that no deformity here or in the distal end of the femur has occurred. There is no limitation in motion and the man is working at the present time—occupation, boilermaker.

CASE VII.—Man, aged twenty-four years. No trauma in history. The trouble began with pain and aching at the knee, which became quite severe, especially at night, when he had been on his feet a great deal during the day.

Films revealed a large area of destruction in the anterior part of the lower end of the left femur (Fig. 17). Although the process lacks the clean-cut, trabeculated appearance of a benign giant-cell tumor, it was felt that these features were absent owing to



FIG. 17.—Case VII. Before Röntgen therapy. (Lateral view.)



FIG. 18.—Case VII. After Röntgen therapy. (Lateral view.)

the rapid growth of the tumor. There was some disagreement as to the diagnosis. The response to Röntgen-ray therapy was prompt. The pain was relieved and the swelling diminished. The tumor became firm to touch and the radiographs (Fig. 18) made later showed an effort at bone regeneration.

These cases of patients with giant-cell tumor in the lower end of the femur are the most important and most satisfactory group. Very frequently the surgical results here are in comparison quite unsatisfactory. Deformity of the joint surface and limitation in motion is common following curettage, and if recurrence takes place or infection develops, these commonly lead to amputation. In all of the cases of giant-cell tumor in the distal end of the femur which we have treated, the tumors were so large that had a curettage

been performed only a shell of the bone would have remained, insufficient for weight-bearing purposes. It has been stated that although the Röntgen-ray may cure giant-cell tumors the period of disability necessary for bringing about firm callus production is so great that surgical treatment is preferable. In the beginning of this work in 1920 that statement seemed to be true, but since 1925, with improvement in technic and the administration of light doses, this statement no longer holds. With the exception of one case, our last five cases of giant-cell tumors of the distal end of the knee have been allowed to be up and around some with the use of a walking Thomas splint, and following their usual occupation, and there has been no real period of disability from the time that treatments were started. It is believed that this is partly responsible for the rapidity of bone regeneration. The patient who is kept flat on his back in bed with the knee immobilized in plaster splints is certainly not going to show so prompt callus production.

*Treatment.*—The question is frequently asked, "What is the dose you employ in the treatment of giant-cell tumors?" The answer is rather unsatisfactory, for there is no standardized method of irradiating these tumors. There is no Röntgen-ray dose. The amount of radiation given to the tumor and the methods of delivering it vary with the case, so that the answer to this question usually is, "It varies with the case."

Few of these tumors respond alike to the same dose of Röntgen-rays. Radiosensitivity varies, as does that of other tumors, with the presence or absence of many factors, which include age of the patient, location of the tumor, rate of growth, and the local effort at growth restraint.

As in other instances, the more cellular, rapidly growing, or malignant a tumor may be, the more prompt is its response to radiation; and frequently the safest plan to follow in Röntgen-ray therapy is first to apply a test dose. In the majority of instances these tumors are comparatively radiosensitive, and seldom is it necessary to employ massive, high-voltage doses. Heavy doses are frequently followed by a severe reaction characterized by redness, swelling, tenderness, pain with an actual expansion of the tumor itself, as shown in the radiographs. In the beginning of this work we believed that this was essential in obtaining a favorable result. We have since found that owing to the susceptibility of these tumors, they can be destroyed through the application of lighter doses which are not followed by this extreme degree of reaction. Bone regeneration seems to follow more promptly when lighter doses are employed. Furthermore, during the severe stage of reaction fracture may occur, and the accompanying pain produces contraction of the muscles, and the tumor may be telescoped over the end of the shaft of the bone in which it occurs.

Special care should be taken during the early stage of the treatment of these tumors to protect the part from injury, and especially to protect the tumor from pressure in a weight-bearing limb, but it is seldom necessary to apply plaster splints, or to hospitalize the patient. Patients have been allowed to be up and around with the use of a walking Thomas splint or

crutches. Later these have been withdrawn and the patient allowed to be about with a cane, and several have gone on earning a living during the period of active treatment.

In the knee-joint cases, and this is the most important group from the practical standpoint, we have given on the average eight or ten treatments, a series consisting of three exposures, the exposures from three or four days to a week apart, the portals consisting in the external, anterior and internal surfaces, using the so-called low voltage technic, 140 kilovolts, 4 milliamperes of current, 4 millimetres of aluminum filters, 12-inch target skin distance, and from 12 to 15 minutes' exposure. An interval of approximately six weeks to two months is allowed to elapse before these treatments are repeated; but a great deal of variation occurs in the dosage and methods of delivering it. The röntgenologist must himself determine the amount to be given in each case at each treatment, and the decision as to how much to give and when to give it can be arrived at only through careful questioning of the patient, examining the part under treatment, and inspection and comparison of the radiographs obtained from time to time.

Patience is essential. A good case for Röntgen therapy with conditions present insuring a good result may be badly damaged through haste and the application of too many heavy doses given too closely together, and our failures to obtain prompt and satisfactory results have often been for this reason. In other instances where Röntgen-ray therapy failed to control the growth and bring about satisfactory ossification we later learned that the original diagnosis of giant-cell tumor was wrong, and that we were really dealing with a malignant atypical bone sarcoma, or a metastatic process. However, it appears that sufficient time has elapsed and the number and variety of cases are large enough to warrant the conclusion that the optimistic statements made in the article referred to above, published in 1924, were fully justified as shown by the course of the above cases since that time.

The writer desires to express his gratitude for the support, encouragement, and advice given by Dr. James Ewing in the earlier stages of this work, without which it probably would not have been undertaken. And no doubt many of those cases under X-ray treatment during that period would have subsequently been operated on, some for amputation, before the final Röntgen-ray results were demonstrable, had it not been for his repeated insistence that sufficient time must be allowed to elapse in each case before the ultimate effects of Röntgen-ray therapy could be determined. Often during the stage of reaction to Röntgen therapy, the appearance of the tumors suggested increased activity of the growths. At other times for over a period of weeks there would be no demonstrable evidence of the beneficial effects of radiation, and no evidence of ossification apparent. It is during such periods that patience is essential. Resorting to surgery or to further radiation, as stated before, may prevent results which might otherwise be very satisfactory.



# RÖNTGEN THERAPY IN CARCINOMA OF THE BREAST

A STATISTICAL STUDY OF 977 PRIVATE CASES

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WE HAVE confined our studies to private cases, because until recently it has been impractical to follow the dispensary cases in the hospitals. We have found private cases very much more coöperative. The 977 cases forming the basis of this study include those patients who were treated between June, 1902, and June, 1927, or a total period of twenty-five years. The last cases in this series have been treated more than three years ago.

Thirty years ago, an individual case of cancer which was cured by X-rays excited much interest. Since then, almost every practitioner has seen the disappearance of cancer in some part of the body, so that now we have become more interested in the general or relative value of the X-rays in various types or locations of cancer. This has led to the preparation of statistics. Most observers dealing with cancer also have seen primary, recurrent, and metastatic carcinoma of the breast disappear as a result of radiation treatment, and enough cases have now accumulated to be of some value as statistics. Unfortunately, any statistical study of radiation in carcinoma of the breast today must include the results of a developing and variable technic. It must always be remembered that technic and clinical judgment count for as much in radiology as in surgery. Better results are being produced today than were produced even ten or five years ago.

A statistical study of the therapeutic results in carcinoma is always difficult because of the variable factors involved and the great difficulty of classification. Unfortunately, the great majority of patients with carcinoma of the breast who are referred to the radiologist are in the inoperable and very advanced stages. Dr. W. J. Mayo says: "In this type of case, radiotherapy is at its best a triumph and a despair. It often does so much good that the patient and the family begin to look for a cure, but failure is the result, and radiotherapy is unjustly brought into disrepute for a meritorious performance."

A direct comparison with surgical statistics is difficult because very few primary cases have been referred for radiation treatment. In the great majority of instances, as the subsequent statistics will show, only the inoperable cases have been referred for primary treatment, and only the more advanced cases for post-operative treatment. Recurrent carcinoma, which

makes up a great part of our cases, is not even included in the usual surgical statistics.

The great variation in the extent of the disease, either primary or recurrent, together with the variability in the degree of malignancy, and the sensitivity to radiation, makes classification extremely difficult. We have, therefore, made use of numerous tables to determine the value under variable circumstances. It is well known that in all surgical clinics many patients are not treated at all because they are beyond any surgical relief, and therefore are not included in surgical statistics, while practically all cases are treated by radiation and we have, therefore, included all.

In most surgical statistics, the cases are classified on the basis of operability. Practically all surgeons, today, consider tumor tissue which is movable and confined to the breast as operable. Most surgeons still consider carcinoma which has invaded only the axilla as operable, but practically none consider a case with supraclavicular involvement as operable.

The end-results are affected not only by the extent of the disease, but by the type of cancer, the rapidity of growth, the age of the patient, the extent of metastasis, the regions invaded, the physical condition of the patient, the duration of the symptoms before operation, or the duration of the recurrence before radiation is begun and the time interval between operation and post-operative treatment. We have, therefore, taken these factors into consideration so far as is practical in making up these statistics. We have previously made statistical reviews of our breast cases in 1925, 1928, and 1929. We are now bringing this review up to June, 1930. In our previous reviews as well as in this review, we counted as dead all patients that could not be traced. Since the 1925 report and in each subsequent report, we have been able to trace some of the missing cases. This has made an improvement in our percentage values. When patients could not be traced we have counted them as living only to the date of our last record.

As shown in the 1929 study we have not found the grading of tumor tissue as to the degree of malignancy as shown by the routine microscopical sections to be of value in making a prognosis (Table I).

TABLE I  
*Sex, Social Status, and Location*

|              | Number       | Per cent.                |               | Number | Per cent. |
|--------------|--------------|--------------------------|---------------|--------|-----------|
| Males.....   | 12           | 1.2                      | Married.....  | 742    | 76        |
| Females..... | 965          | 98.8                     | Single.....   | 235    | 24        |
| Total.....   | 977          | 100.                     |               | 977    | 100       |
|              | Right breast | involved in 455 cases or | 46 per cent.  |        |           |
|              | Left breast  | involved in 469 cases or | 48 per cent.  |        |           |
|              | Both breasts | involved in 53 cases or  | 6 per cent.   |        |           |
|              | Total        | 977                      | 100 per cent. |        |           |

This table shows that while carcinoma of the breast in males is rare, it still makes up over 1 per cent., and, since 6 per cent. of the cases show involvement of both breasts, the presence of a tumor in each breast does not rule out carcinoma.

TABLE II  
*Conditions Which First Attracted Attention to the Tumor*

|        |                       |                |
|--------|-----------------------|----------------|
| Lump   | 55 per cent. of cases | } 91 per cent. |
| Pain   | 21 per cent. of cases |                |
| Injury | 15 per cent. of cases |                |

The remaining 9 per cent. gave as the first complaint the following symptoms:

|                             |                           |
|-----------------------------|---------------------------|
| Stinging sensations.        | Tender axilla—neck.       |
| Eczema of nipple.           | Dimpled skin.             |
| Bleeding nipple.            | Sinus in breast.          |
| Discharge from nipple.      | Pigmented mole.           |
| Ulceration of nipple.       | Pain right under abdomen. |
| Soreness in nipple.         | Rheumatism in back, etc.  |
| Retraction of nipple.       | Swollen arm.              |
| Increase in size of breast. | Cough.                    |
| Lump in axilla.             | Dyspnoea.                 |
| Lump in neck.               | Cachexia.                 |
| Abscessed breast.           | Anæmia.                   |

This table shows, of special importance, that a lump or pain is the first symptom in 76 per cent. of the cases, and that traumatism should lead to a careful examination and follow-up if negative. It also shows that any of the twenty-five symptoms mentioned should lead the physician to make a careful examination of the breasts.

TABLE III  
*Time Intervening Between the First Symptom and Active Treatment by Either Operation or Radiation*  
(Average 16.2 months)

| Time                | Cases | Time                        | Cases |
|---------------------|-------|-----------------------------|-------|
| 1 month . . . . .   | 103   | 2 years . . . . .           | 110   |
| 2 months . . . . .  | 95    | 3 years . . . . .           | 107   |
| 3 months . . . . .  | 41    | 4 years . . . . .           | 22    |
| 4 months . . . . .  | 60    | 5 years . . . . .           | 20    |
| 5 months . . . . .  | 67    | 6 years . . . . .           | 12    |
| 6 months . . . . .  | 68    | 7 years . . . . .           | 7     |
| 7 months . . . . .  | 39    | 8 years . . . . .           | 8     |
| 8 months . . . . .  | 22    | 9 years . . . . .           | 4     |
| 9 months . . . . .  | 11    | 10 years and over . . . . . | 3     |
| 10 months . . . . . | 22    |                             |       |
| 11 months . . . . . | 23    | Total . . . . .             | 960   |
| 12 months . . . . . | 116   |                             |       |

No record in seventeen of the cases.

# RÖNTGEN THERAPY OF BREAST CARCINOMA

The average duration of symptoms during 16.2 months before operation or radiation in the 960 cases in which this fact is recorded shows, in general, the advanced type with which we have dealt. It should also stimulate us all to make more of an effort to educate the public and the profession as to the early symptoms of cancer of the breast, and the importance of skillful and active treatment at once. It is rather discouraging to note that only approximately 69 per cent. received active treatment within twelve months, and 10 per cent. within one month. It must also be noted that all of these cases were treated more than three years ago. We note more alertness now.

TABLE IV  
*Age Incidence*

| Years         | No. of cases | Years         | No. of cases |
|---------------|--------------|---------------|--------------|
| 16.....       | 1            | 55 to 60..... | 96           |
| 18.....       | 1            | 60 to 65..... | 104          |
| 20 to 30..... | 24           | 65 to 70..... | 50           |
| 30 to 40..... | 125          | 70 to 75..... | 38           |
| 40 to 45..... | 161          | 75 to 80..... | 18           |
| 45 to 50..... | 192          | 80 to 85..... | 8            |
| 50 to 55..... | 159          |               |              |

65.2 per cent. of all cases between ages of thirty and fifty-five. Only  $2\frac{2}{3}$  per cent. were under thirty years of age. Total 977 cases.

TABLE V  
*Average Time Duration from Operation to Recurrence*  
(One Year and 7 Months)

| Recurrence within | Cases | Recurrence within | Cases |
|-------------------|-------|-------------------|-------|
| 1 week.....       | 4     | 12 months.....    | 40    |
| 2 weeks.....      | 10    | 1½ years.....     | 33    |
| 3 weeks.....      | 8     | 2 years.....      | 39    |
| 4 weeks.....      | 34    | 3 years.....      | 21    |
| 5 weeks.....      | 3     | 4 years.....      | 20    |
| 6 weeks.....      | 5     | 5 years.....      | 9     |
| 7 weeks.....      | 1     | 6 years.....      | 7     |
| 8 weeks.....      | 21    | 7 years.....      | 6     |
| 3 months.....     | 21    | 8 years.....      | 6     |
| 4 months.....     | 29    | 9 years.....      | 2     |
| 5 months.....     | 16    | 10 years.....     | 3     |
| 6 months.....     | 27    | 11 years.....     | 1     |
| 7 months.....     | 14    | 12 years.....     | 1     |
| 8 months.....     | 11    | 13 years.....     | 1     |
| 9 months.....     | 11    | 15 years.....     | 2     |
| 10 months.....    | 10    | 18 years.....     | 1     |
| 11 months.....    | 2     |                   |       |
|                   |       | Total.....        | 419   |

Recently, a woman discovered a tumor in her breast at 8 A.M.; and at 10 A.M. she was in the surgeon's office and at 11 A.M. she was in our office for radiation treatment because the diagnosis was mastitis, and now she is well.

It is to be noted that approximately 64 per cent. of the 419 cases had their recurrences within a year, while the latest recurrence occurred after eighteen years. This patient was operated upon eighteen years previously by Dr. W. W. Keen and was referred for treatment of the recurrence by Doctor Keen and Dr. John B. Deaver. At the time of the recurrence in the right breast, a tumor had also developed in the left breast, which was amputated by Doctor Deaver five weeks before coming to us. There was a recurrence in the operative scar on the left also, showing that the resistance to cancer was at a low ebb. The recurrences showed marked reduction after radiation but the patient was seventy-seven years of age and died of cardiac disease four months after beginning treatment. This table also shows that there was a total of thirty cases out of four hundred and nineteen, or approximately 7 per cent., in which the recurrence occurred more than five years after operation.

TABLE VI  
*Time Interval Between the First Sign of Recurrence and the Beginning of  
Radiation Treatment*  
(Average 6.6 months)

| Time          | Cases | Time           | Cases |
|---------------|-------|----------------|-------|
| 2 weeks.....  | 10    | 8 months.....  | 9     |
| 3 weeks.....  | 12    | 9 months.....  | 9     |
| 4 weeks.....  | 58    | 10 months..... | 3     |
| 5 weeks.....  | 4     | 11 months..... | 2     |
| 6 weeks.....  | 11    | 12 months..... | 64    |
| 7 weeks.....  | 3     | 1½ years.....  | 11    |
| 8 weeks.....  | 63    | 2 years.....   | 10    |
| 3 months..... | 50    | 3 years.....   | 3     |
| 4 months..... | 19    | 4 years.....   | 3     |
| 5 months..... | 25    | 5 years.....   | 4     |
| 6 months..... | 35    |                |       |
| 7 months..... | 11    | Total.....     | 419   |

This average delay of 6.6 months in obtaining radiation treatment seems unwise and unnecessary. It would seem that the delay is either due to a lack of follow-up inspection, or too great assurance given to the patient that there will be no recurrence, or that the surgeon is unwilling to recognize the recurrence.

Based upon our observations it would seem that if these patients had all received routine, thorough and skillful post-operative irradiation, beginning within two or three weeks after operation, nearly all could have avoided at least a local recurrence. One cannot always avoid metastasis, because distant metastasis may have taken place long before the operation.

# RÖNTGEN THERAPY OF BREAST CARCINOMA

TABLE VII

*Average Time Intervening Between Operation and Röntgen Treatment in Recurrent Group*  
(Average 22 months)

| Treatment started | No. of cases | Treatment started | No. of cases |
|-------------------|--------------|-------------------|--------------|
| 3 weeks.....      | 4            | 1½ years.....     | 49           |
| 4 weeks.....      | 7            | 2 years.....      | 41           |
| 5 weeks.....      | 1            | 3 years.....      | 30           |
| 6 weeks.....      | 6            | 4 years.....      | 20           |
| 7 weeks.....      | 5            | 5 years.....      | 17           |
| 8 weeks.....      | 25           | 6 years.....      | 6            |
| 3 months.....     | 24           | 7 years.....      | 6            |
| 4 months.....     | 21           | 8 years.....      | 6            |
| 5 months.....     | 23           | 9 years.....      | 2            |
| 6 months.....     | 21           | 10 years.....     | 3            |
| 7 months.....     | 11           | 11 years.....     | 1            |
| 8 months.....     | 18           | 12 years.....     | 1            |
| 9 months.....     | 8            | 13 years.....     | 1            |
| 10 months.....    | 12           | 15 years.....     | 2            |
| 11 months.....    | 7            | 18 years.....     | 1            |
| 12 months.....    | 40           |                   |              |
|                   |              | Total.....        | 419          |

Table VIII shows seventy-nine cases in which there were one or more operations for recurrence before being referred for irradiation of the new recurrence. Of this group, twenty-seven, or 34 per cent., of the cases remained well three years, and fifteen, or 19 per cent., of the cases remained well five years and over. This would seem to indicate the advisability of thorough irradiation locally and in the adjacent tissues where metastases are

TABLE VIII

*Showing Operations for Recurrences Before Being Treated by Irradiation*

39 cases, 1 operation before second recurrence  
23 cases, 2 operations before third recurrence  
8 cases, 3 operations before fourth recurrence  
5 cases, 4 operations before fifth recurrence  
4 cases, 5 operations before sixth recurrence

—  
Total 79 cases

likely to be found as a routine post-operative procedure, but especially at the earliest sign of recurrence. A 39 per cent., three-year, and a 20 per cent., five-year salvage after one or more operations for recurrence is pretty high.

The largest group of cases was referred for post-operative treatment within two weeks after operation, but all within eight weeks. We believe that practically all cases can and should be referred for post-operative irradiation.

TABLE IX

*Average Time Intervening between Operation and Röntgen Treatment in Post-operative Group*  
(Average 4.21 weeks)

| Treatment started | No. of cases |
|-------------------|--------------|
| 2 weeks.....      | 77           |
| 3 weeks.....      | 37           |
| 4 weeks.....      | 46           |
| 5 weeks.....      | 15           |
| 6 weeks.....      | 24           |
| 7 weeks.....      | 16           |
| 8 weeks.....      | 36           |
| Total.....        | 251          |

tion within two weeks after operation. The object of this irradiation is to destroy any cancer cells that may have been left behind, either locally or in the neighboring lymphatics. We are quite sure that the earlier these cases are treated the better will be the results providing the treatment is adapted to the patient's general condition.

TABLE X

*Classification of Types and Extent of Involvement in 977 Cases of Cancer of the Breast*

|   | Cases | Per cent. |
|---|-------|-----------|
| a. Pre-operative and post-operative cases.....                        | 88    | 9         |
| b. Post-operative.....  | 251   | 26        |
| c. Recurrent with metastasis; involvement of bones, glands, or chest. | 419   | 43        |
| d. Primary inoperable cases.....                                      | 167   | 17        |
| e. Primary operable.....  | 52    | 5         |
| Total.....  | 977   | 100       |

It should be noted in Table X that nearly twice as many cases were sent on account of recurrences and metastases as for post-operative irradiation. We believe there will be very few recurrences, if patients are given skillful and thorough post-operative irradiation.

Of the 123 cases in which no microscopical section was obtained, forty-seven were recurrent and metastatic so that seventy-six or 7.7 per cent. of the total might have the diagnosis disputed, except on clinical evidence. Of these seventy-six cases, thirteen were primary operable, in which operation was refused or was inadvisable because of some physical condition, leaving sixty-three cases in which the surgeon's judgment must be accepted.

In 136 cases no biopsy was made because the disease was clearly malignant and inoperable.

# RÖNTGEN THERAPY OF BREAST CARCINOMA

TABLE XI  
*Histological Classification*

|  | Cases |
|--|-------|
| None obtained (including primary operable—only 13 cases were clinically doubtful)            | 123   |
| None made (inoperable primary and recurrent).....  | 136   |
| "Carcinoma".....   | 224   |
| "Malignant".....   | 129   |
| "Fibroadenoma" (these cases were sent to us because of later recurrence and metastasis)..... | 18    |
| Colloid carcinoma.....   | 2     |
| Paget's disease.....   | 8     |
| Adenocarcinoma.....  | 79    |
| Medullary carcinoma.....   | 13    |
| Scirrhus carcinoma.....  | 163   |
| Carcinoma simplex.....   | 41    |
| "Benign tumor" (sent to us later because of recurrence and metastasis).....                  | 11    |
| * Carcinoma en cuirasse.....   | 29    |
| Papilliferous cyst carcinoma.....  | 1     |
| Total.....   | 977   |

\* The diagnosis submitted by the surgeon or pathologist.

Of the eighteen cases diagnosed as "fibroadenoma" at the time of the operation and all of which were sent to us because of recurrences or metastasis, nine died of carcinoma.

In the discussion of the 1925 paper, it was suggested that this group of "fibroadenomata" should be eliminated—because it was not understood that they were recurrent cases. A recurrence in our opinion is as good proof of malignancy as a microscopical diagnosis. The experiences with these latter twenty-nine cases ("fibroadenoma," eighteen, and "benign tumor," eleven) shows that one cannot always depend upon the microscopical report, due, of course, to the fact that the malignant portion of the tumor was not brought under the microscope.

The eleven cases diagnosed at the time of operation microscopically as "benign tumor" were sent to us on account of recurrences or metastasis, and of these, eight cases died of the disease.

TABLE XII  
*Classification of Types and Extent of Involvement in 977 Private Patients with Cancer of the Breast*

The groups under each subdivision are classified after the fashion of the generally accepted surgical tables:

|                |   |
|----------------|---|
| Group I.....   | Early operable—no glands involved                   |
| Group II.....  | Late operable with glands involved                  |
| Group III..... | Local recurrence—operable                           |
| Group IV.....  | Local recurrence, inoperable, primary and secondary |



## a. Cases receiving both pre-operative and post-operative treatment

| Group      |    | Before operation | After operation             | No. of cases | Per cent. |
|------------|----|------------------|-----------------------------|--------------|-----------|
| A          | I  | No glands.....   | No glands.....              | 20           | 22        |
| B          | II | Glands.....      | No glands.....              | 37           | 43        |
| C          | IV | No glands.....   | Glands (not removable)..... | 19           | 21        |
| D          | IV | Glands.....      | Glands (not removable)..... | 12           | 14        |
| Total..... |    |                  |                             | 88           | 9*        |

## b. Cases receiving post-operative treatment

|            |    |   |     |     |
|------------|----|---|-----|-----|
| E          | I  | No glands at operation, and no glands when radiation was begun  | 55  | 22  |
| F          | II | Glands at operation, but no glands when radiation was begun.... | 99  | 40  |
| G          | IV | Glands at operation, and glands when radiation was begun.....   | 72  | 29  |
| H          | IV | No glands at operation, glands when radiation was begun.....    | 25  | 9   |
| Total..... |    |   | 251 | 26* |

## c. Recurrent cases treated by radiation

|            |     |   |     |     |
|------------|-----|---|-----|-----|
| I          | III | Local recurrence.....   | 62  | 15  |
| J          | IV  | Local recurrence in glands, axilla and supraclavicular region.....          | 67  | 16  |
| K          | IV  | Local recurrence metastasis, mediastinum—lungs.....                         | 30  | 7   |
| L          | IV  | Local recurrence in axilla and supraclavicular and mediastinal regions..... | 219 | 53  |
| M          | IV  | Local lesion and metastasis to spine and other bones.....                   | 14  | 3   |
| N          | IV  | Metastasis, mediastinum, lungs and bones.....                               | 27  | 6   |
| Total..... |     |   | 419 | 43* |

## d. Primary inoperable cases treated by radiation

|                 |    |   |     |     |
|-----------------|----|---|-----|-----|
| O               | IV | Fixed to skin or glands with axillary supraclavicular and mediastinal distribution . . . . .      | 112 | 67  |
| P               | IV | Fixed to skin or glands with axillary, supraclavicular involvement plus bone metastasis . . . . . | 28  | 17  |
| Q               | IV | Made operable without chest metastasis . . . . .  | 19  | 11  |
| R               | IV | Made operable with chest (palliative operation) . . . . .   | 5   | 3   |
| S               | IV | Removed by electrocoagulation . . . . .   | 3   | 2   |
| Total . . . . . |    |   | 167 | 17* |

## e. Primary operable cases treated by radiation

|            |   |   |       |       |
|------------|---|---|-------|-------|
| V          | I | Primary operable, unquestionably malignant (refused or physically not fit)..... | 39    | 75    |
| T          | I | Primary operable, questionably malignant, (3 per cent. of all cases).....       | 13    | 25    |
|            |   |   | <hr/> | <hr/> |
| Total..... |   |   | 52    | 5*    |

\* Per cent. of 977 cases.

Referring to Table XIII, which is the general summary of all the work, it will be observed that in the *Pre-operative and Post-operative Group*, the three-year recoveries vary from 65 to 50 per cent. with a general average of

Other Details and Abbreviated Words Are Shown in Table XII

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59 per cent., and five-year recoveries vary from 62 to 12 per cent., with a general average of 50 per cent. This is less than the recoveries in the post-operative group, but it must be remembered that nearly all of these cases were advanced and doubtfully operable or totally "inoperable" before irradiation. Therefore, five-year recoveries of 50 per cent. is very good. Pre-operative irradiation is probably advisable in all but the strictly localized cases, but we advise pre-operative irradiation especially when there is skin ulceration or supraclavicular glands.

*Post-operative irradiation* is proven to be of very definite value, as is shown in this group in which the three-year recoveries vary from 96 per cent. to 37 per cent., depending upon the extent of the disease, giving a general average of 62 per cent. The five-year recoveries vary according to the extent of the disease from 87 per cent. to 30 per cent., but with a general average of  $53\frac{1}{2}$  per cent. In the group in which there was glandular involvement at the time of operation which are usually considered the late operable cases, 55 per cent. were well at the end of five years. This is about two and a half times as many recoveries as occur from operation alone, and should leave no doubt as to the advisability of post-operative irradiation in all cases of cancer of the breast.

We realize that these results differ from those reported by Harrington, in which his results seem to indicate that the irradiation added very little. We made inquiry concerning this and found that the more advanced cases were referred for post-operative treatment; that the radiation treatment in these early years was not well developed at the clinic; and finally, and most important, that as Harrington says, "In a large percentage of cases in which the Röntgen-ray was used initial treatment at the clinic and subsequent treatment elsewhere had been given." These factors, we believe, explain the marked difference in observations by Harrington and ourselves, for we attach great importance to a careful technic.

*Recurrent and Metastatic Carcinoma* forms the largest group, and these recurrences were recognized from two weeks to five years before being sent for treatment, but with an average of 6.6 months, some of which had from one to five operations for recurrences before the disease for which we irradiated; and nearly all had associated metastasis. With such material our three-year recoveries varied from 56 per cent. to 14 per cent., but with a general average of 39 per cent. The five-year recoveries varied from 47 per cent. to 4 per cent., but with a five-year recovery of 20 per cent. of all cases treated for recurrence and metastasis.

*Primary Inoperable Carcinoma* shows 167 cases treated with three-year recoveries of from 84 per cent. to 35 per cent. and with a general average of 43 per cent. The five-year recoveries vary from 58 to 25 per cent., but with a general average of  $30\frac{1}{2}$  per cent. of all cases treated. This is a better percentage of five-year recoveries in inoperable cases than from *operation alone in the operable cases with axillary involvement*.

*The Primary Operable Group of Carcinoma of the breast*, in which there



TABLE XV

*Statistical Study of Radiation Therapy in Carcinoma of the Breast (231 Cases) Duration of Life after the Beginning of Treatment—1922 to June 1, 1927*  
During the Period of the Use of the High Voltage X-rays and the "Saturation Method" (Pfahler)

| Other Details and Abbreviated Words Are Shown in Table XII                      |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
|---|--|-----------------------|---|---|----|---|----|---|----|-------|---------------|----------|---------------|----------|-----|--------|---|
| Group   | Months<br>alive  | Number of years alive |   |   |    |   |    |   |    | Total | Alive 3 years |          | Alive 5 years |          |     |        |   |
|   |  | 6                     | 8 | 1 | 1½ | 2 | 2½ | 3 | 3½ |       | 4             | 5        | 6             | 7        | 8   | Number | % |
| a. Cases receiving both pre-operative and post-operative irradiation (39 cases) |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| A I   | Op. no invol. of gl.                                     | 2                     | — | — | 1  | — | 1  | 1 | 1  | 1     | 8             | 5 of 8   | 62            | 3 of 4   | 75  |        |   |
| B II  | Op. with invol. of gl.                                   | —                     | 2 | 2 | 2  | 2 | 2  | 2 | 4  | 1     | 15            | 11 of 15 | 73            | 7 of 11  | 63  |        |   |
| C IV  | No gl. at op.—gl. after op.                              | 1                     | 2 | — | 1  | — | —  | 2 | —  | —     | 8             | 4 of 8   | 50            | 2 of 4   | 50  |        |   |
| D IV  | Gl. at op. and gl. after op.                             | 1                     | — | 1 | —  | 3 | —  | 1 | —  | —     | 8             | 5 of 8   | 62            | 1 of 5   | 20  |        |   |
| b. Cases receiving post-operative irradiation (59 cases)                        |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| Total and average   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 39  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| E II  | No gl. op.—no gl. when irradi.                           | —                     | — | — | 1  | — | 4  | — | 6  | 5     | 23            | 22 of 23 | 95            | 14 of 15 | 93  |        |   |
| F II  | Gl. op.—no gl. when irradi.                              | —                     | 2 | 1 | 3  | — | —  | — | 2  | 4     | 16            | 10 of 16 | 62            | 8 of 14  | 57  |        |   |
| G IV  | Gl. op.—gl. when irradi.                                 | 1                     | 1 | — | 2  | — | 2  | — | 1  | 1     | 11            | 6 of 11  | 54            | 3 of 4   | 75  |        |   |
| H IV  | No gl. op.—gl. when irradi.                              | 1                     | — | 2 | —  | 1 | 3  | — | —  | —     | 9             | 5 of 9   | 55            | 2 of 3   | 66  |        |   |
| c. Recurrent cases treated by irradiation (88 cases)                            |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| Total and average   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 59  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| I III   | Local recurrence.  | —                     | — | — | 2  | 1 | 2  | — | 2  | 2     | 11            | 8 of 11  | 72            | 4 of 8   | 50  |        |   |
| J IV  | Rec. gl. ax. and s. c.                                   | 2                     | 1 | 2 | 1  | — | 4  | — | 1  | 1     | 14            | 7 of 14  | 50            | 2 of 9   | 22  |        |   |
| K IV  | Rec. met. med. and lungs.                                | 2                     | 2 | 2 | 2  | — | 1  | — | 1  | —     | 11            | 3 of 11  | 27            | 1 of 10  | 10  |        |   |
| L IV  | Rec. ax. and s. c. and med.                              | 5                     | 2 | 6 | 4  | 2 | —  | — | 3  | 5     | 30            | 11 of 30 | 36            | 6 of 13  | 46  |        |   |
| M IV  | Loc. les., met. spine and bones.                         | —                     | 2 | 1 | 2  | — | 1  | — | —  | 2     | 8             | 3 of 8   | 37            | 2 of 5   | 40  |        |   |
| N IV  | Met. med.—lungs and bones.                               | 4                     | — | 2 | 2  | 1 | 1  | — | 1  | 1     | 14            | 3 of 14  | 21            | 1 of 11  | 9   |        |   |
| d. Primary inoperable cases treated by irradiation (48 cases)                   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| Total and average   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 88  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| O IV  | Fix. sk. or gl. and ax. s. c. and med.                   | 7                     | — | 6 | 1  | 3 | —  | 1 | —  | 2     | 25            | 8 of 25  | 32            | 5 of 21  | 23  |        |   |
| P IV  | Fix. sk. or gl. and ax. s. c. and b. met.                | 2                     | — | 1 | 3  | — | —  | 2 | 4  | 2     | 16            | 10 of 16 | 62            | 4 of 9   | 44  |        |   |
| Q IV  | Made op. without chest met.                              | 1                     | — | — | —  | — | —  | 2 | —  | 1     | 5             | 4 of 5   | 80            | 2 of 3   | 66  |        |   |
| R IV  | Made op. with chest (pall. op.).                         | 1                     | — | — | —  | — | —  | — | —  | —     | 1             | 0 of 1   | 0             | 0 of 1   | 0   |        |   |
| S IV  | Remov. by electrocoagulation.                            | —                     | — | — | —  | — | —  | 1 | —  | —     | 1             | 1 of 1   | 100           | 0 of 1   | 0   |        |   |
| e. Primary operable cases treated by irradiation (17 cases)                     |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| Total and average   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 48  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| V I   | Prim. op. unques. malig. (refused or phys. not fit)      | —                     | — | — | —  | — | 1  | — | 6  | 2     | 15            | 14 of 15 | 93            | 8 of 10  | 80  |        |   |
| T I   | Prim. op. questionable malig. (3 per cent. of all cases) | —                     | — | — | —  | — | —  | — | —  | 1     | 2             | 2 of 2   | 100           | 2 of 2   | 100 |        |   |
| Total and average   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 17  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| Grand total and average   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 251   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 16 of 17  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 77 of 163   |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 94  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 56  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 83  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |
| 47  |  |                       |   |   |    |   |    |   |    |       |               |          |               |          |     |        |   |

was no doubt about the clinical diagnosis, numbered only thirty-nine cases. These either refused operation or were physically unfit. Of these, there were 89 per cent. of three-year recoveries and 85 per cent. of five-year recoveries.

*Total Values.*—We have tried to classify the cases in a manner in which one could make a fair comparison, but it may be of value to summarize the entire group as cancer material and estimate in this manner the chances of recovery that a private patient has had in the past twenty-five years by a combination of surgery and irradiation. Taking, therefore, the whole material of 977 cases, there has been a recovery of 50 per cent. for a period of three years and 36 per cent. for a period of five years. This gives a far less gloomy picture of the results of the treatment of carcinoma of the breast than is usually presented, but, if all the knowledge which is now available is properly utilized, this percentage should be doubled, at least for private cases in which one gets better coöperation than is obtained in the hospital clinic case. The difference in the number of cases under treatment in the five years as compared with the three-year column is due to the fact that some of these cases were not referred more than three or four years ago.

Having made a general analysis of the radiation value in carcinoma of the breast during a period of twenty-five years, it seemed important to determine whether the statistics would justify our clinical opinion of definite improvement in our results since we have been using the high voltage rays and the "saturation method" combined as compared with the results obtained previously. Table XIV shows the results obtained during the twenty years preceding this technic, and during which time all improvements in radiology were also utilized as they were developed. We have, therefore, also classified the cases treated since 1922 by this later technic and apparatus, as is shown in Table XV.

TABLE XVI  
*Comparative Results before 1922 (Low Voltage) and  
after 1922 (High Voltage and "Saturation")*

| Group  | 1902 to 1922<br>Low voltage—<br>variable technic |                      | 1922 to 1927<br>High voltage and<br>"saturation" |                      |
|--|--|----------------------|--|----------------------|
|  | 3 years<br>Per cent.                             | 5 years<br>Per cent. | 3 years<br>Per cent.                             | 5 years<br>Per cent. |
| Pre-operative and post-operative—all classes . . . . . | 55   | 47                   | 64   | 54                   |
| Post-operative with no ax. glands . . . . .            | 96   | 84                   | 95   | 93                   |
| Post-operative with ax. glands . . . . .               | 63   | 55                   | 62   | 57                   |
| Post-operative—all classes . . . . .                   | 59   | 49                   | 73   | 75                   |
| Recurrent and metastatic—all classes . . . . .         | 39   | 19                   | 40   | 28½                  |
| Primary inoperable—all classes . . . . .               | 42   | 30                   | 48   | 32                   |
| Primary operable—clinically positive . . . . .         | 87   | 87                   | 93   | 80                   |
| Average results in all cases treated . . . . .         | 48   | 33                   | 56   | 47                   |

Table XVI shows a very definite improvement in all classes as a result of our improvement in apparatus and technic. It shows further that with

both pre-operative and post-operative treatment according to modern technic even when many cases were inoperable, 54 per cent. showed five-year recovery.

It shows further that a patient who goes to the surgeon before the axillary glands are involved has a 93 per cent. chance of five-year recovery, providing she gets thorough and skillful post-operative irradiation, and if there are axillary glands there is still a chance of 57 per cent. with our most modern methods.

The *Recurrent and Metastatic* cases still show a 28½ per cent. salvage after five years.

The *Primary Inoperable* case need not be abandoned as hopeless when there is a 32 per cent. five-year salvage.

With regard to the *Primary Operable* cases, we recommend operation when this is practical as the shortest and most certain way out of trouble, but when this is not practical, we may still expect an 80 per cent. recovery from thorough and skillful irradiation.

A very striking demonstration of progress is shown in the last line of Table XVI, in which the general results in all classes of cases of carcinoma of the breast treated between 1902 to 1922 are compared with those treated from 1922 to 1927. The latter group was treated by the more modern technic which shows 47 per cent. of five-year recoveries as compared with a general average of 33 per cent. before 1922. It is also most encouraging that a case of cancer of the breast in the general average today has a 47 per cent. chance of cure.

TABLE XVII

*Statistical Study in Twelve Cases of Carcinoma of the Breast in Males*

| No. of cases | Age | Duration of tumor | Operation  | Metastasis                | Recurrence before rad. | Alive              | Dead                |
|--------------|-----|-------------------|--|---------------------------|------------------------|--------------------|---------------------|
| I            | 55  | 5½ years          | 5 years before rad.                                | To rt. ax., s. clav. reg. | 1 year                 | 1 year             | Yes                 |
| II           | 68  | 1 year            | 2 months before rad.                               | To rt. and lt. axilla     | 4 weeks                | 1 year             | Yes                 |
| III          | 78  | 9 months          | 3 weeks before rad.                                | To lt. ax., s. clav. reg. | None                   | 1 year             | Yes                 |
| IV           | 55  | 2 weeks           | 6 days before rad.                                 | None                      | None                   | 2 years, 11 months | Yes                 |
| V            | 60  | 3 years           | 1 year before rad.                                 | To rt. ax. and chest      | 5 months               | 1 year             | Yes                 |
| VI           | 32  | 2 months          | 4 weeks  | None                      | None                   | 7 years            | No                  |
| VII          | 60  | 3½ years          | 3 years before rad.                                | To rt. ax., s. clav. reg. | 2 years                | 11 years           | No                  |
| VIII         | 74  | 8½ years          | 8 years before rad.                                | To rt. ax.                | 1 year                 | 3 years            | Yes—myocarditis     |
| IX           | 65  | 4 weeks           | 2 weeks before rad.                                | None                      | None                   | 6 years            | No                  |
| X            | 73  | 4 weeks           | Pre- and post-op. tr. 2 wks.                       | To rt. ax.                | None                   | 5 years            | Yes—apoplexy        |
| XI           | 60  | 1½ years          | 1 year before rad.                                 | To rt. ax., s. clav. reg. | 5 months               | 9 months           | Yes                 |
| XII          | 50  | 6 months          | X-ray treat. electrocoag. X-ray treat. after dest. | To rt. ax., s. clav. reg. | None                   | 8 years            | Yes—cardiac disease |

*Carcinoma of the Breast in Males.*—Judd and Morse have recently reviewed the former reports and have added seventeen cases of carcinoma of the breast in males. In general, a little more than 1 per cent. of carcinomata of the breast occurs in males. We have twelve cases in this series, and have not noticed any appreciable difference in our results as compared with carcinoma in the female. Judd and Morse believe that they are more malignant and have not found the röntgenological treatment of appreciable value. We have seen recurrences and metastasis disappear under irradiation. Table XVII shows definite value in irradiation.

Nine of these cases were proven carcinoma by microscopical examination. In the remaining three cases, none was obtained, but they all died within one year of carcinoma.

Of the twelve cases, six were recurrent, four post-operative, and one received pre- and post-operative treatment, one was primary, with a protruding growth beyond the skin (No. XII), this part was removed by electrocoagulation, but not the whole breast.

Case No. IV developed a recurrence in the axilla two years after operation and irradiation, which yielded to further irradiation, but a fibrous nodule remained. He consulted a surgeon in a distant city who urged immediate operation, which was done by him on the succeeding day and two days later he died.

Six cases lived three years—50 per cent.

Five cases lived five years and over—41 per cent.

Three cases are living at present—25 per cent., six, seven, and eleven years respectively.

#### SUMMARY

The review of 977 cases treated during a period of twenty-five years shows:

1.—*Pre-operative and post-operative irradiation* will render many inoperable and doubtfully operable cases operable.

2.—*Post-operative irradiation* gives a general average of all cases of 53½ per cent. five-year recoveries, and with the more modern technic this is increased to 75 per cent. In the operable group, in which the disease had extended only to the axillary glands, there were 55 per cent. of five-year recoveries, and with the more modern technic 57 per cent. after five years.

3.—*Recurrent and metastatic carcinoma* gave a general average of 20 per cent. of five-year recoveries and 28½ per cent. when only those treated by the modern methods are considered.

4.—*Primary inoperable carcinoma* gave 30½ per cent. of five-year recoveries, which shows that if a patient cannot be operated upon there is still considerable hope from thorough irradiation.

5.—Only thirty-nine cases of primary operable carcinoma of the breast were treated. These were undoubted clinical carcinoma but unfit for operation or refused operation, but these showed 85 per cent. of five-year recoveries. We recommend operation in all operable cases, to be followed by irradiation.



# RESULTS OBTAINED WITH CARCINOMA UTERI TREATED BY RÖNTGEN-RAYS FROM 1915-1925

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FROM THE ERLANGEN RÖNTGEN INSTITUTE

IN THIS Ewing Cancer Tribute, I have thought it opportune to publish the results and the conclusions thereof in the care of those patients who had been treated during the years 1915-1925 for cancer of the uterus.

The treatment consisted, in this decade, chiefly in Röntgen therapy; only in special cases were small quantities of radium energy given in addition. This was done when the dose necessary for the destruction of cancerous tissue could be brought only with great difficulty to the site of the tumor.

For the statistics under discussion, this was the case with cancer of the corpus uteri and with those tumors of the cervix which, on account of a descensus uteri, have slipped into the vagina, so that the central ray of a field of incidence applied to the suprasymphyseal region can scarcely reach the tumor. It was only in the second half of this decade that I used systematically an additional radium dose with cancer of the corpus uteri, while, during the first half, also with this form of cancer, Röntgen therapy alone was employed.

I. For this decade the technic of irradiation was, on principle, the same, though, since 1920, due to important improvements of the apparatus, the time of irradiation became much shorter.

The dose applied, the "cancer dose," is 110 per cent. of the HED, *i.e.*, Hauteinheitsdosis, or unit skin dose (USD).

The value of the USD in its original definition can be expressed by the standardized international  $r$  units; thus, a value of about 600  $r$  is obtained. But it is to be taken into consideration that this value is valid only if the dose is applied at one or two sittings in the course of forty-eight hours. Suppose the dose is distributed over a long time, the same amount of  $r$  units would actually produce a smaller biological effect, for it has been known a long time that distributing a dose over some period means a diminution of biological action. The reason for this lies in the recuperative faculty of the cells being able to compensate the action of small Röntgen-ray quantities. The lowest limit of irreparable injuries of the cancer cell lies with 60 per cent. of USD = 360  $r$ .

This is why I think it necessary with cancer therapy to apply the dose wanted for destruction of cancer, if possible, at one sitting, or at least in the course of forty-eight hours. Only in this way is it possible to load the surrounding tissue with the least possible quantity of rays. During the past years experiments have been made over and over again with the purpose of distributing the Röntgen quantities over a series of days. It resulted

from these experiments with certainty that the total dose to be applied to a tumor must be much greater than the total doses administered by means of my technic, if a success shall be guaranteed.

With regard to the technic, it would be the same whether the irradiation at one sitting or the distribution over a long time is used, if only the loading of healthy tissue with Röntgen-rays would be the same in both cases. But this is noways the case, as we have seen.

It is certain, without further argumentation, that the recuperative faculty of the cancer cell whose characteristic is rapid growth must be different from that of normal body cells distinguished by normal slow metabolism.

We know from a series of fundamental experiments that cells having slow metabolism, cumulate Röntgen-rays in a much stronger degree, or, to put it in a different way, those cells take a much longer time than cancer cells to compensate small Röntgen injuries.

Therefore, with the method of fractioned doses, the organism is only apparently more spared than with the other one; actually, the healthy tissue will cumulate the rays in a much higher degree than the cancer cells. The final destruction of cancer cells thus is paid for by much greater injury of healthy tissue. Clinical experience has proved this incontestably. If the treatment is given with fractioned doses, induration is seen sooner and in a more pronounced degree than with the treatment at one sitting. All this justifies my holding fast to the principle of applying the dose at one sitting.

As to the technic of irradiation, we proceed in the following way: At first, the primary tumor is irradiated by concentrating Röntgen-rays onto it from a series of fields of incidence of the size of six by eight centimetres. The technic being often described,\* may be supposed to be known. Eight weeks later, the parametria are treated. In the period with which these statistics deal, there is also a difference in so far as, prior to 1920, the treatment of parametria was divided in two sittings, first one side being irradiated, and, after six to eight weeks, the second one.

Since 1920 (up to the present time) both parametria are irradiated at one sitting in the course of forty-eight hours.

II. The principles according to which my statistics are drawn up are the following:

All positive cases of cancer received for treatment at the clinic are followed up in the statistics whether the treatment could be finished or not. They are considered to be "cured" only when, five years after the treatment is finished, the patients are free of symptoms and able to work according to their age.

There are two groups: *symptom-free* (healthy) cases and *lost* ones.

Under the heading of "lost cases" are included:

(a) All those who have died whether of carcinoma or of an intercurrent disease, even if at autopsy all cancerous growth had disappeared; and

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\* Radiology, vol. v, p. 500.

(b) Those cases who showed local or metastatic cancer or whose general health implied the existence of latent metastases.

Besides, the material is grouped in *operable* and *inoperable* cases. Those are considered to be operable whose cancerous growth is still restricted to its primary site; inoperable, those with affected lymphatic glands or with symptoms of general dissemination. According to the strict statistical principles drawn up by Winter, cases hopeless from the beginning are also included.

Recurrences after operation form a separate group.

Stress must be laid on the fact that all cases are followed up. Those very few (four) which could not be traced, because they had moved abroad, are counted as dead.

The statistics of cancer of the uterus of the Erlangen Röntgen Institute for the decade of 1915–1925 covering over 956 patients, yield the following results:

(a) *Cancer of Cervix Uteri*

(1) Operable cases.— $125:75 = 60$  per cent. symptom-free and able to work according to their age.

(2) Inoperable cases.— $712:86 = 12$  per cent. symptom-free and able to work according to their age.

(b) *Adeno-carcinoma of Corpus Uteri*

(1) Operable cases.— $59:41 = 69.5$  per cent. symptom-free and able to work according to their age.

(2) Inoperable cases.— $160:5 = 8.3$  per cent. symptom-free and able to work according to their age.

The importance of these statistics lies in the fact that a considerable number of patients (956) were treated with nearly the same technic in the course of ten years, while the statistics of many other institutes are dealing with frequently changing methods.

Of course, the technic became more and more improved every year, but the principle drawn up in 1915 of applying the cancer dose, if possible, at one sitting or in the course of forty-eight hours, was followed ever since. Improvements were made especially with regard to electrical conditions, with the result that the time a treatment took became much shorter in a later period (1922–1925) than it was in the first one (1915–1919), as mentioned before.

As the most essential improvement of the second half of this decade dealt with in the statistics is to be considered the fore- and after-treatment,\* not less important in the sense of auxiliary therapy is *copper treatment*.

The value of these improvements is clearly shown by partial statistics which are won under the same conditions as the total one and deal with the years 1922–1925. For this period, the following percentages are obtained five years after treatment was finished:

*Operable Cases*

Cancer of cervix uteri, 66.6 per cent.

Cancer of corpus uteri, 80 per cent.

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\* Radiology, vol. i, p. 74.

# RESULTS RÖNTGEN-RAY TREATMENT CANCER UTERI

## *Inoperable Cases*

Cancer of cervix uteri, 15 per cent.

Cancer of corpus uteri, 14 per cent.

A short description of the *technic of coppering* may follow: The idea which led to the elaboration of this technic was to produce secondary radiation in the tissue by metallic particles introduced by means of iontophoresis.

For cancer of cervix uteri the technic is the following: As anode a copper tube is used which is shaped in the form of the rose of a watering-can. The copper tube is uncovered for about three to five centimetres of its length, the remainder being protected by hard rubber. It is wrapped in cotton wool and gauze in order to form a kind of sponge electrode, which, on introduction to the vagina, fits closely to the mucous membrane. If the vagina is not sufficiently plugged in this way, small burns of the mucosa may result (Joule's heat). The portion of the rubber tube which lies outside the vagina is armed with a pinch-cock and is connected with a douche can which supplies a solution of cuprum selenicum (5 in very small doses—about 15–20 drops per minute.) Care must be taken that the whole plugging is sufficiently moist, and that, at the same time, no liquid escapes from the vagina. The hollow cathode, consisting of clay, is filled with a solution of rock salt; the size of this electrode which is put on the abdomen is about 300–400 square centimetres. Good contact with the skin is essential. The current is applied from an accumulator of 8 volts. A resistance is inserted in the electric circuit, permitting the regulation of the tension; the intensity is read from a milliamperemeter.

In order to regulate the circuit of the current from the vaginal anode to the cathode, a careful insulation of the skin is to be observed by putting a broad layer of grease over the symphysis and round about the cathode. If insulation and connection are correct, only a weak current is passing, when joined up; the pointer of the milliamperemeter rises slowly. The normal average intensity amounts to about 40–50 milliamperes. Experience has shown that the use of from 200–250 milliamperè-hours is most suitable. When 300 milliamperè-hours are surpassed, injuries may occur. We have never seen injuries up to 250 milliamperes, nor even irritation of kidneys, in spite of the fact that copper may be found in urine, or even in saliva, about two days after copper treatment.

Copper treatment is administered to all cases of cancer of cervix uteri; eventually, also, to cases of cancer of corpus uteri, as well as with all other ulcerated cancers.

The physical action of coppering consists in iontophoresis and electrolysis. Thus, the tissue lying between cathode and anode is imbibed with copper salt solution, most strongly in the neighborhood of the cathode. Besides, copper ions are transported by means of electrolysis in the direction of the cathode. As we may presume that the walls of cells do not offer any resistance to the copper ions, copper particles are supposed to enter the cells. Near the anode, selenic acid is being liberated so that an irritative action is produced in the superficial layers.

With regard to being an auxiliary to Röntgen therapy, secondary radiation produced by copper ions is of minor importance only. According to measurements, the local increase of the so-treated tissue in susceptibility to Röntgen-rays is about 20 per cent. at the utmost. Nor can the oligodynamic action of copper be of particular consequence, but the clinical value, consisting principally in a *disinfecting action* in the sense of *deep disinfect-*

tion, and becoming evident in accelerated regression of the tumor as well as in more rapid healing up (cicatrization and formation of normal tissue), is of prime importance.

In one of my former papers,\* I have pointed out that the infection of a tumor cannot be taken too seriously. At the Radium Institute in Paris the same statement has been made, *i.e.*, that infected cancerous growths have much worse chances to be healed than non-infected ones. Further investigations have shown that radiosensitiveness of a cancer cell is diminished while that of the surrounding tissue is increased. Thus, radiosensitiveness of healthy and diseased tissue becomes nearly the same. It results, hereof, that susceptibility reduced by infection cannot be compensated by augmenting the dose, for healthy tissue, extremely sensitized by infection, will answer with serious injury. Our clinical investigations correspond with those published by Lacassagne, from the Radium Institute of Paris. The importance of the problem follows from the proposition of this author first to perform a deep disinfection with infected tumors before beginning the treatment, though there is no doubt that precious time is lost during disinfecting treatment.

As I have already shown, we are well entitled to see in copper treatment an especially favorable method of deep disinfection. It is from this reason that the action of coppering is so propitious with infected tumors.

To ascertain the value of copper treatment by drawing up statistics is not easy; even if one tries to compare as many homogeneous cases as possible, it might be objected that, judging from the local findings and the general health of the patient, it is impossible to foretell which turn the disease will take. Besides, it would be necessary to subdue all patients to exactly the same conditions of treatment, in order to be able to pass an incontestable opinion on the action of copper treatment. But, being convinced of its value, I cannot make up my mind to exclude patients from this therapy for experiment's sake. I, therefore, have for this comparison only those cases at my disposal which have been treated with Röntgen-rays before copper treatment was inaugurated and a second group from a later period treated by copper iontophoresis. In the course of time, though I have not changed the principles of my method, the deep action of radiation and the time of application have been altered by technical improvements. Even the general conditions of life are not the same with these patients. That is why I can render my results only with certain reservations though I have chosen patients whom I have personally examined.

I contrast two groups, each of sixty cases of cancer of cervix uteri (squamous-cell carcinoma), whose clinical findings could be characterized as inoperable, but still localized to the pelvis: infiltration of both parametria, in all cases streptococcus hæmolyticus positive.

The percentage of cure is:

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\* Acta Radiologica, vol. vii, p. 675.

## RESULTS RÖNTGEN-RAY TREATMENT CANCER UTERI

### *Three Years After the Treatment Is Finished*

Group I (without copper treatment), 8 per cent.

Group II (with copper treatment), 16 per cent.

### *Five Years After the Treatment Is Finished*

Group I (without copper treatment), 6.3 per cent.

Group II (with copper treatment), 13 per cent.

There is certainly an evident difference, but these statistics must by no means be overvalued, as clinical homogeneousness is difficult to judge. As to infiltration of parametria, for instance, nobody can decide, with certainty, whether this infiltration is cancerous or only inflammatory. According to my experiences, this difference with regard to the chance of a cure is not essential with exclusive radiotherapy as any inflammatory process means a great complication for this therapy. If, however, Röntgen therapy is combined with an efficient disinfecting treatment, the results obtained with inflammatory infiltration will be much better than with cancerous infiltration. But, anyhow, the value of any therapeutic method is ascertained by definite cures.

III. Repeatedly, I have, with regard to radiotherapy, pointed out the *importance of life conditions and of systematic after-care*. In 1923, I could report statistical results\* with cases well followed up, having the same clinical findings. The difference which became manifest in the results obtained with two groups I had formed, was produced by the condition of life under which these patients lived after having had Röntgen therapy. With one group of patients all that could be done was to hospitalize them for a long time or to send them to a sanatorium for completion of cure. Others, again, had all they wanted as to rest, diet and nursing at their homes. When it was impossible to give them the benefit of long hospitalization, these women had to return to their jobs in poor or even miserable home conditions after the treatment was finished and when they were just beginning to recover. At that time (1923) we stated, three years after treatment was finished, a difference of results from 42 : 22 per cent. and four years afterwards from 41 : 15 per cent.

With cases I recently have controlled personally with regard to this problem, the difference was no longer so marked as with the material followed up in 1923, when the conditions of life in Germany were still affected by war and inflation times. But the results won with a series of 140 patients having the same clinical findings show, nevertheless, the following difference four years after the treatment was finished:

Group I (good conditions of life), 46 per cent. symptom-free and able to work.

Group II (bad conditions of life), 32 per cent. symptom-free and able to work.

All the same, these results are very important and have led me to insist on good after-care. As conditions of life have become better these last

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\* Strahlentherapie, Bd. xv, p. 770.

years, the benefit of hospitalizing patients for some weeks can be conferred to a broader mass of patients than before. After-care, as I have pointed out elsewhere,† must aid the body to eliminate the products of degeneration. Mechanical cleaning is obtained by disinfecting irrigations; resorption from the vagina, not being of much importance, plays a rôle anyhow. For those masses of decayed cells which have been swept off by the blood-stream, something can be done by medication with the purpose of accelerating metabolism. Sulphur administered either *per os* or by means of intravenous injections has proved to be very successful. Arsenical preparations, formerly greatly appreciated with cancer therapy, are of essential importance only with patients in poor systemic condition. With women who tend to grow stout, arsenical medication is not wise. Change of altitude has proved to have a very favorable action, the influence of altitude, which has an accelerating effect on metabolism, being particularly propitious for the elimination of degeneration products. It is of prime importance to watch the weight curve after radiation therapy. Loss of weight, when conditions of life are otherwise satisfactory, is a bad symptom.

IV. Though statistics demonstrate clearly the value of special care after treatment for cancer, it is very unsatisfactory that one knows so little about the relations of systemic conditions and cancer. That is the reason why any procedure to cure the body of the cancerous disease offers so little chance of success. The disappointments one experiences over and over again with initial cancerous growths prove this above all.

The reason for this limit of our efficiency lies partly in early dissemination of cancer from ever so small a primary tumor. I recently was able to state by autopsy in six cases that the cancerous growth in the corpus uteri and in its surroundings was completely healed up, but that those patients had died of distant metastases.

Thus, the size of a cancerous growth, in as far as the tumor may be characterized as being localized, does not permit one to draw any definite conclusion as to prognosis, though, in general, it is correct to presume that the bigger the primary tumor, the worse the prognosis.

Neither are systemic condition nor looks of the patient determinant with regard to the final result of treatment. Every one knows those patients who, seemingly in blooming health, come with an initial cancer of uterus for treatment, but die in the course of one to two years, while others of apparently cachectic condition, a definite cure is obtained.

I have drawn up some statistics of cancer of the cervix uteri dealing with the fate of young women (operable cases). It yields, five years after the treatment is finished, the following results:

Group I (1916-1921), symptom-free and able to work, 38 per cent., instead of 56 per cent. of the total average.

Group II (1922-1925), symptom-free and able to work, 50 per cent., instead of 66 per cent. of the total average.

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† Radiology, vol. i, p. 74.

These results fall considerably short of the standard. That they cannot be explained by chance is shown by the great surgical statistics. Here, also, cancerous growth with young women has a much more grave prognosis *quoad sanationem* than with women over forty years of age. The reasons for this are unknown: another example for the fact that the relations between destruction of cancer and collaboration of the total organism to obtain a definite cure, still offer a wide field of study.

V. The efficiency of any radiotherapeutic method becomes manifest after surgical operation. In the subsequent statistics I have assembled all those cases of cancer of uterus on which a Wertheim operation had been performed at some time or other, and which came with recurrence for Röntgen treatment. The clinical quality of these cases differs widely, so that really a series of subdivisions would be necessary. But to be loyal to the principle of the all-comprising statistics of Winter, all those cases are included which are hopeless from the beginning, though they are a burden especially for this statistics table.

*Results Obtained with Recurrences After Operation for Cancer of the Uterus  
by Röntgen Therapy*

118 patients, three to four years after treatment symptom-free and able to work  
20 = 17 per cent.

104 patients, five to six years after treatment symptom-free and able to work  
10 = 9, 6 per cent.

59 patients, eight to nine years after treatment symptom-free and able to work  
4 = 6, 7 per cent.

VI. I cannot close the discussion of my statistics without referring to a special circumstance. The percentages of cure, obtained for localized cancerous growth of the uterus, already attain a considerable height today; the more desolate, on the contrary, are the results with the so-called inoperable cases. Though we may be satisfied in thinking that without radiation therapy these cases would all be lost, a cure percentage of 12 per cent. is still unsatisfactory. Although, with our methods of treatment, we expect to improve the results from year to year, still only a small per cent. can be added.

From the total statistics of those cases of inoperable cancer where the cancerous growth had extended over the pelvis without having formed distant metastases—a cure percentage of 22 is obtained. This seems to be the best result possible. The difference between operable and inoperable cases remains great. This fact proves clearly that besides further improving our *methods* of cancer therapy we must try to reach cancer cases earlier. Thus, the demand of the years to come will be: *Wider information among mankind as to early symptoms of cancer and the possibility of curing an initial cancerous growth.*

In this propaganda to fight cancer, the United States of America takes the lead in an aggressive way.



# THE TREATMENT OF CANCER OF THE BODY OF THE UTERUS BY RADIATION

By CURTIS F. BURNAM, M.D.

OF BALTIMORE, MD.

FROM THE HOWARD A. KELLY HOSPITAL

CANCER of the body of the uterus is, with very rare exception, an adenocarcinoma and tends to metastasize somewhat more slowly than that of the cervix. Visceral and distant metastases are, however, much commoner than in the epidermoid carcinoma of the cervix. The disease is rare when compared to cervical cancer. The ratio between these two groups in our records is as one to fourteen.

Old age is a predisposing cause. Patients with uterine body cancers are much older on the average than those afflicted with the cervical, ovarian, and other gynecological carcinomas. In 165 patients of this group, treated in the clinic of the Howard A. Kelly Hospital, the average age was fifty-seven years. This age probably is some years beyond the average age of all women with this particular form of cancer, because most of the patients were sent to us for radiation because of some physical disability—not infrequently old age itself. In the early cases, the average age was fifty-nine years; in the advanced cases, fifty-eight years; in the recurrent cases, fifty-one years; in the metastatic cases, fifty and a half years. The oldest woman in the group was eighty and the youngest twenty-eight years. Dr. Leda J. Stacy, in 333 cases treated at the Mayo Clinic, notes that it is fairly frequent in younger women—10.51 per cent. of her cases were under forty-five years of age. In our series, there were nineteen cases under forty-five years of age, exactly 11.5 per cent.

Heredity probably is an important predisposing cause but it is rather difficult to prove this on clinical material. There is a distinct tendency, with these patients, to develop cancer in some other part of the body of an entirely different type; and, occasionally, two distinct cancers are found at the same time in the same patient. As to the influence of race on the frequency of this cancer. There is a large negro population in Baltimore and, in our clinic, we see a great deal of cancer in the negro. It, therefore, is somewhat surprising to find only two negroes in the entire group of 165 cases. It is our impression that cervix cancer is relatively much more frequent in the negro than in the Caucasian and that it can be attributed to the prevalence among the negroes of the venereal diseases and, also, to the average greater number of pregnancies and poorer obstetrical care at labor.

In the literature, there are current and frequently repeated statements that cancer of the uterus is much more frequent in women with fibroid tumors, in those suffering from sterility, and in those who are unmarried. Without accurate information as to the percentage of fibroids in all women, of sterility in all married women, and of spinsterhood in general, our small

group of cases is of limited value in throwing light on the importance of these factors. However, my impression is that they have little, if any, etiological significance. As only a small percentage of our cases was subjected to surgical operation, the determination of fibroids had to be made by clinical examination—a somewhat uncertain method. In the entire group, fibroids definitely were found only in 12 per cent. Doctor Stacy, in 269 operated cases, found 33.45 per cent. fibroids. C. C. Norris and Vogt in 115 cases, observed this complication in 21 per cent. James Ewing quotes Klob to the effect that 50 per cent. of all women over fifty have uterine fibroids; and that 20 per cent. of all over thirty-five are similarly affected. Uterine fibromata are much commoner in negroes than in whites but, apparently, body cancers are much rarer, and the reverse should be the case if fibroids cause or favor cancer.

Sterility does seem to be a predisposing, or, at least, an associated condition. In 127 records, where this question is clearly taken up, there were fifty-eight women who had children and sixty-nine who had none. In these women, there was, therefore, a 55 per cent. sterility. All of them had been married for years. Most of those who had children were multipara; the greatest number of children in any one case was sixteen.

Out of the entire group, twenty-six were married, 15.7 per cent. This does not seem a high percentage of unmarried women, but it may be, if only unmarried women of the age of our patients are considered.

Whenever the diagnosis of cancer of the body is established and the local conditions in the pelvis determined, there remains the obligation to examine the patient exhaustively for abdominal and general metastases. This is much more urgent than in cervical cancer.

*Treatment.*—It is convenient in considering treatment to divide the cases into the early operable, the late border-line and inoperable, the recurrent after operation, and the metastatic.

When the disease is limited to the uterus, there are two possible methods of successful treatment. Hysterectomy, long in use, is accompanied by a lower mortality and a higher percentage of permanent cures than the same procedure has yielded in treating cancer of the cervix. Recently, Stacy, Heyman, Schreiner, and others have reported methods and results in treating these early cases with radium alone. These reports point to the possibilities of the non-operative methods and Heyman, in particular, records a five-year cure rate comparable with that obtained by surgical operation. He, nevertheless, still feels that, unless there is some general contra-indication, such as old age and corpulence, very high blood-pressure, organic heart disease, nephritis, or diabetes, operation is the method of choice.

When the disease has extended beyond the uterus, there is very little field for operative interference, but there is still definite hope of a cure by radiation. We have had two patients who belong in the inoperable extensive group where a combination of operation and radiation has been of value. In one, in addition to a very large carcinoma of the body of the uterus, there was bilateral involvement of both ovaries. The patient was

in rather poor general condition and, at operation, the ovarian carcinomas were found densely adherent to surrounding structures. A rapid removal of both ovarian masses was carried out and, in place of removing the uterus, radium treatment was given to take care of that part of the disease. During the convalescence, additional radium radiation was given by crossfire method to the entire pelvis. The uterus, originally the size of a three and a half months' pregnancy, is now quite small and free of disease. The patient also seems quite well after two years. The second patient had a small, freely movable uterus which was removed along with the tubes and ovaries by abdominal operation, but a packet of glands was found over the iliac vessels—one of these was removed and found to be cancerous. After recovery from the operation, a systematic and careful radiation of the involved iliac region was carried out and this patient—now five years later—seems free of cancer. Such cases as these must be the great exceptions and the shock and lowered resistance from operations, in most of the inoperable cases, would only lessen the chances of benefiting by radiation.

When the disease has extended by metastasis beyond the first regional glands, operation obviously is contra-indicated. Exactly the same treatment holds true of all cases which have recurred after surgical removal of the uterus.

*Operative Technic.*—It does not fall within the scope of this paper to discuss the details of surgical treatment of cancer of the body of the uterus. There is a lower primary mortality from vaginal hysterectomy than from abdominal hysterectomy. The former method, however, in addition to yielding a smaller percentage of permanent cures, has the disadvantage of being applicable only to those cases where the pelvis is roomy, the uterus small and perfectly movable. The abdominal operation always should include removal of the tubes, ovaries, cervix and top of the vagina. There is a very definite primary mortality associated with abdominal panhysterectomy for corpus carcinoma. In our own series of twenty-seven cases where abdominal hysterectomy was resorted to, the primary death rate was 9 per cent. So far as general examination showed, these cases all were in good condition and were good operative risks. Doctor Stacy in a series of 239 cases from the Mayo Clinic reports a primary mortality of six per cent. The reports from the literature indicate a primary mortality running from about 6 per cent. to 15 per cent.

*Technic of Radiation.*—In the early cases, and in all cases so far as the disease of the uterine body is concerned, our chief reliance has been on intra-uterine radium treatment. There has been no primary mortality or serious complications.

Our source of radiation has been radon in a glass tube or bulb, surrounded by a millimetre of brass and three millimetres of rubber. We usually employ from one curie to three curies of radon, divided into from four to six equal parts. The tubes, to which strings are attached, are introduced into the uterine cavity and a dosage of from two and one half to three gram hours

is given. The dosage is not surpassed unless the uterus is a very large one and the cavity very extensive. Crossfire radiation, either by radium or by X-ray, should be given with great care and mainly to the iliac glands and lateral walls of the pelvis. There is real danger of intestinal injuries if this radiation is super-added to the uterine radiation by central exposure. In the very large, inoperable cases, and in the metastatic cases, the conditions are so variable that no definite plan can be laid out to cover groups of cases. Each patient must be individualized and the method decided upon which promises the most complete treatment. A great deal of this treatment is by crossfire radiation from the surface of the body. Unless several grams of radium are available, it is preferable to use X-ray. Where the radium is available, it is decidedly more efficacious.

The radiation of post-operative cases demands special consideration. Very frequently the small intestine has become adherent to the vaginal scar and the radiation which is given directly to the vault of the vagina should be of a very mild character. The lower vaginal wall, which is a frequent point of metastasis, can be treated more vigorously. The regional gland regions should be treated by crossfiring, as already has been referred to above.

Intra-uterine treatment is usually given under nitrous oxide anæsthesia, with the usual antiseptic precautions for intra-uterine handling. The patient is kept in the hospital for a few days until it is evident that complications will not take place. The discharge usually ceases within five or six weeks. Some of the larger uteri decrease as markedly as do fibroid uteri after radiation. After from ten to twelve weeks, the patient is brought back to the clinic, given a second anæsthesia, and thoroughly curetted. If no malignancy is found, no further treatment is given. If cancer still is present, either a hysterectomy or a repetition of the treatment is carried out. The former method is preferable unless the general condition contra-indicates any operative procedure.

The patients should be put in full possession of the facts as to their conditions and instructed to keep in touch with the clinic and report back at stated intervals, even when there are no symptoms.

*Results.*—It is not a simple matter to secure from the literature accurate data as to the percentage of permanent cures of cancer of the body of the uterus. Our own material from the operative standpoint is quite small. Heyman collecting from a number of reports notes 323 operations with 58.8 per cent. of cure. By radium alone, in fifty-two cases, there was 50 per cent. of five-year cure at the Radiumhemmet in Stockholm. John G. Clark reports 42 per cent. of three-year cures. Norris and Vogt, 44 per cent. cures. Stacy reports 269 cases treated by hysterectomy of whom she was able to trace 215. Of these, 108—50.2 per cent.—were living at the end of four years. A little more than 40 per cent. could be tabulated as living if all the cases unheard from were dead. However, sixteen patients who died subsequent to the operation died of other causes than cancer and this, of course, would raise the operable cure rate. Out of thirty-two patients treated by

radium alone, she was able to trace twenty-five, all but two of whom had died from the disease.

Our own cases are grouped under four headings: first, comparatively early, possibly operative cases; second, advanced inoperable cases; third, recurrent cases; fourth, cases already presenting metastases.

*Comparatively Early, Possibly Operative Cases.*—In this group, the cases should be subdivided into those treated by operation alone, by radium alone, by radium and operation, and by operation and radium. It has been our impression up until quite recently that if a patient were in normal general physical condition and the uterus freely movable, operation alone, or operation followed by radiation, was the method of choice. As a consequence, with two or three exceptions where a patient positively refused operative interference, all the patients have been treated by operation, whether radiation was given prior to, or subsequent to, the operation or not given at all. The patients who have been treated with radium alone have been those where a technical operative condition existed but the general condition of the patient made operation unusually hazardous. The chief disabilities in our group were old age and corpulence, high blood-pressure, organic heart disease, diabetes, and nephritis.

Eleven cases were treated by operation alone; forty-six cases by radium alone; eleven cases by radium and operation; and five cases by operation and radium.

*Cases Treated by Operation Alone.*—There were eleven of these cases, five less than five years old all are still living. Of the six remaining cases, three are living, one died from operation, one died from recurrence, and one has been lost sight of. Known living after five years represents 50 per cent. of the total. Excluding the case lost sight of from consideration, the operative five-year cure rate is 60 per cent.

*Cases Treated by Radium Alone.*—There were forty-six of these cases. Of these forty-six cases, nineteen have been treated within five years and will be excluded from consideration. Of the remaining twenty-seven cases treated prior to five years ago, fifteen are living, seven are dead from the disease, and five from other causes. Of the living cases, five have just passed the five-year period, one, six years, one, seven years, one, eight years, four, nine years, two, ten years, and one, twelve years. Of the seven cases dying from recurrence, practically all had metastases; one lived one year, two lived two years, two, three years, one, four years, and one, seven years after the treatments. Of the patients who died from other causes than cancer, four died of apoplexy, and one of diabetes. One of the patients lived a year, two for three years, and one for four years.

After five years, of twenty-seven patients, fifteen are living and well, and twelve are dead, making a rate of 55 per cent. living and 45 per cent. dead. If we exclude from our list the patients known to have died of other causes than cancer, the cure rate is 69 per cent. If the cases dying of other causes than cancer and with no evidence of cancer are put in the cured list, the rate of cure would be 74 per cent.

*Cases Treated by Radium and Operation.*—There were eleven of these cases. Of these eleven cases, two have been treated within five years and will be excluded from consideration. Of the remaining nine cases treated prior to five years ago, five are living and well, two died of recurrence, one from the operation, and one has been lost sight of. The percentage living is 55.5 per cent. and if the lost-sight-of case is excluded, the cure rate would be 62.5 per cent. In most of these patients, operation was performed a few days after radiation; but in two cases, a period of 60 days elapsed between the radiation and the hysterectomy; and, although curettage had demonstrated the disease prior to operation, the uterus after removal was found clear of cancer on most careful pathological study.

*Cases Treated by Operation and Radium.*—There were five of these cases. Of these five cases, one has been treated within five years and will be excluded from consideration. Of the remaining four, all are well. One, however, had a recurrence which, at a subsequent treatment, was cleared by the radium.

*Advanced Inoperable Cases.*—By inoperability is meant local extensions without demonstrable metastases which render complete removal impossible. The extensions may be either lateral or over the vaginal walls. A number of these patients were given only palliative treatment. At the present time, we would be very much inclined to treat everyone by a plan which aimed to cure. Omitting from consideration fifteen cases treated within the last five years, there remain thirty-one. Of these thirty-one cases, we have been unable to trace four. Sixteen died within two years; three lived for longer than two years; three lived for longer than three years; and one lived for five years. Four cases are living and well, so far as clinical examination discloses, after five years. The first of these patients, well for five years, had a complicating fibroid. The uterus was the size of a six months' pregnancy. There was fixation to the left pelvic wall. The histological grading was No. 1. The second case was inoperable as the entire uterus was involved and the condition extended down on to the vaginal wall. There was no fibroid present but the uterus was the size of a four months' pregnancy. Within three years, the uterus was of normal size and at the end of five years the patient still is well. The histological grading was No. 3. The third case has already been referred to and is well six years after treatment. Inoperability here was due to local metastatic glands on the pelvic wall found at the time of hysterectomy. The fourth case was inoperable because of fixation through the right broad ligament to the pelvic wall. This was grade No. 2 and the cure has lasted for five years. The five-year cure rate is 12.9 per cent. in this group. Taking the entire group of forty-six cases, and taking one year as the period of cure, the rate is 21 per cent.

*Recurrent Cases.*—Out of a total of thirty such patients, twenty-four have been treated more than five years ago. Twenty-two are dead; two are living and well. Of those that died, one lived three years, and one lived seven years; the others all died within two years of the time of the treatment. One of the cured cases has been well for six years and one for nine

years. The cure rate is 8.3 per cent. Our results in this group have been disappointing. When the patients came to us in most of the cases the disease seemed limited to the vagina and, practically without exception, the vaginal metastases cleared up. In some cases these were followed by local recurrences and in some by abdominal metastases. All died of the disease.

*Cases Already Presenting Metastases.*—There were eleven of these patients. In not one was a cure obtained. The metastases have been mainly to the pelvic glands and to the abdominal viscera and glands. In most of these patients, there was no attempt made to treat the whole disease but merely to relieve the chief complaint—usually pain. In a patient at present under observation, a large pelvic mass has disappeared and an upper abdominal metastasis has almost disappeared. In the very nature of things, however, the extensive metastatic cases are hopeless from the standpoint of cure. All of these patients of whom our records are complete died within two years of the time of the first treatment.

*General Consideration.*—Taking all cases, operable, inoperable, recurrent and metastatic which were treated prior to five years ago, there are included 112. Of these, ninety-one have died and twenty-one are living. We have not included in the living any cases except those known to be free of the disease. As already has been noted in the operable group, a number of patients died after some years of other causes than cancer. I have not included in these 112 cases those treated in any other way than by radium. The cure rate for the entire group is 18.7 per cent.

A study of our cases does not give us a great deal of encouragement in attempting either to prognose the outcome or to determine the radio-sensibility by grading of the cases. We have observed extensive metastases with grade No. 1's, we likewise have seen grade No. 4's which long have remained local. Our five-year cures represent all four grades.

As with cancer everywhere, the chief factor in determining the probability of cure treatment is the extent of the disease, the earlier the patient comes for treatment, the greater the likelihood of cure.

In operable cancers of the body of the uterus, radiation offers a method of treatment comparable to the best surgical treatment in its permanent results. It obviates, to a large measure, at least, primary mortality and is applicable to a large number of patients who are bad surgical risks.

Radiation offers a possibility of cure in a considerable percentage of inoperable and recurrent cancers of the body of the uterus.

In metastatic cancer, radiation can be a valuable palliative remedy, relieving pain, hæmorrhage, and probably prolonging life.

Pre-operative radiation does not increase the hazards of operation, and post-operative radiation would seem to be a logical procedure in many cases.

Where there is lateral trouble, evident on examination, and a doubt as to whether it is malignant or not, operation is preferable to radiation.

# THE COMBINED RADIUM AND RÖNTGEN TREATMENT OF CANCER OF THE CERVIX UTERI

BY JAMES HEYMAN, M.D.

OF STOCKHOLM, SWEDEN

FROM THE RADIUMHEMMET OF STOCKHOLM.

IN THE early years of gynecological radiotherapy there were constant discussions as to the limits of the zone in which radium was therapeutically effective. It was frequently observed that carcinomata which were strictly limited to the cervix yielded better results than those where the cancer had spread to parametria and glands. This fact was in the first place considered to be due to an insufficient depth dose, the cancer cells at a certain distance from the radium not receiving a sufficient dose. True, the experience of recent years has taught us that an effective radiological treatment is by no means a problem of dosage alone, in the sense that it is only a matter of applying the greatest possible radiation intensity to all layers of the tumor, though it is natural to assume that in some cases an incomplete cure in intra-genital radium treatment must be due to an insufficient depth dose. One is led to this assumption by the fact that not infrequently the cervical tumor itself disappears after treatment while the cancer continues to invade the parametrium and the glands. A more efficacious radiation of the parametria in these cases ought therefore to improve the results. The question of homogeneous irradiation of the pelvis is still a subject under discussion in gynecological radiotherapy.

Not long after Forssell, in 1913, had elaborated our present technic in the radium treatment of cancer of the cervix, we found that we were unable to attain the desired therapeutic effect in the parametria by increasing either the radium quantity or the duration of irradiation. These procedures only led to such an increase of the surface dose that injuries to the tissues in the neighborhood of the focus resulted especially to the bladder and rectum.

We learned that an aggregate vaginal and intra-uterine dose of about six 900 milligram element hours (115 milligram radium element for sixty hours) could not be exceeded without risk.

In order to obtain a more effective irradiation of the parametria it would have been necessary either to alter the technic in the intragenital application or to combine the intragenital application or to combine the intragenital treatment with irradiation of the parametria from some other entrance field.

The former of these alternatives, particularly the possibility of establishing a better relationship between surface and deep dosage through heavier filtration, we considered unwise to adopt, however, at that time. This was partly owing to the fact that we had only relatively small quantities of radium at our disposal, but the main reason was that we felt disinclined to depart



from a technic which held out such promising results before it had been tested on a larger number of cases.

The introduction of deep Röntgen therapy opened up new roads for parametric irradiation. In Germany, about fifteen years ago, the homogeneous irradiation of the pelvis by Röntgen-rays was the dominating question in gynæcological radiotherapy. This was partly owing to the difficulties this country encountered in procuring radium during and after the war. It is scarcely any exaggeration to say that the endeavor of the German gynæcologists to obtain a homogeneous Röntgen irradiation of the pelvis has been one of the most important incentives to the elaboration of modern deep Röntgen therapy (Seitz and Wintz, Krönig and Friedric, Warnekros and Dessauer).

As soon as Radiumhemmet, in the beginning of 1918, had obtained its first outfit for deep Röntgen therapy, the combined Röntgen and radium treatment of cervical cancer was tried in a large number of cases of cervical cancer. In the first instance these were chosen from among those where the previous radium treatment had failed (Rö. I).

During the period 1914-1925, 200 out of 885 cases were treated in this way and every new contribution to the Röntgen technic stimulated us to further efforts. The results, however, have been depressing. In only a few of these cases has a permanent cure been obtained whether there was a question of local or parametric recurrences or of metastases. Occasionally the Röntgen treatment may have inhibited the process or alleviated the pains for a short time, but the effect has been only temporary. A carcinoma which is not cured by our routine radium treatment is practically always refractory to Röntgen rays. This has also been our experience in recent years since we have been using a heavier filtration (filter equivalent to three millimeters of copper).

The above cases, however, are mentioned only in passing as they were not subjected to Röntgen treatment combined with the radium, but received Röntgen treatment only subsequently to radium, as a last resort. The aim of the present investigation is rather to find out whether Röntgen irradiation of the parametria given in direct connection with radium has been a valuable therapeutic adjunct or not. That question must be settled by comparing the end-results in two series of cases, one treated solely by radium, the other treated both by radium and Röntgen rays.

The difficulty in an investigation of this nature lies in the fact that one must have two relatively large series of cases for comparison, observed for at least five years. Furthermore the initial material must be equivalent and the radium technic the same in the two series. Investigations hitherto published on this subject do not seem to me to fulfil these conditions. Our experiences may therefore be of interest, the more so, as, on the one hand, the combined radium-Röntgen treatment is at the present time the form of treatment most in use, and, on the other, because our first impression of the combined therapy was not altogether favorable.

## TREATMENT OF CANCER OF CERVIX UTERI

I have mentioned before on different occasions (*Jour. of Obstet. and Gyn. of the Brit. Emp.*, vol. xxxi, No. 1; *Acta Radiologica*, vol. x, fasc. I, No. 53; and *Proc. of the Royal Soc. of Med.*, vol. xxii) that we tested the combined treatment for a few years but later restricted it to cases with large glandular metastases. The reason for this was mainly that in examining the primary results we were unable to find that the Röntgen treatment had brought about any improvement. A contributory cause was the occurrence now and then of cases of Röntgen cachexia undoubtedly due to a too forced Röntgen treatment. To what extent our reported views of the value of parametric Röntgen application must be corrected will be clear from the following account of the five-year results now available.

Our experiments with combined radium and Röntgen treatment were carried out mainly during 1919 and 1920. A smaller number of cases was treated during 1918, 1921, and in the beginning of 1922. During 1918–1920 our radium technic remained practically unchanged. In 1921 we began our therapeutic attempts at a modified radium treatment, of which an account was published in *Acta Obstet. et Gyn., Scand.*, vol. ix, fasc. 1–4. This modification consisted in giving two instead of three applications of radium. Only a few of the cases thus treated are included in the following statistics. As no other important change in our radium technic has occurred simultaneously with the Röntgen experiments, it may be assumed with fairly great probability that variations, if any, in the therapeutic results may be ascribed to the parametric Röntgen irradiation.

During the period 1918–1922 inclusive, 168 (36.8 per cent.) of a total number of 457 cases of cancer of the cervix admitted for treatment have been treated with combined radium and Röntgen irradiation. This will in what follows be called the combined treatment.

Table I shows the distribution of cases.

The cure result of the combined treatment on the five-year basis is forty-nine cured out of 168 treated. If we now compare this result with the five-year result for the cases numbering 289 treated from the start solely by radium during the same period (1918–1922 inclusive) we find: With radium alone, 21.8 per cent. five-year cures; with combined treatment, 29.2 per cent. five-year cures.

Before venturing upon any conclusions from this comparison, it will be necessary to show that the initial material in the two series is approximately equivalent.

During the period 1918–1922 inclusive, the cases were distributed as follows:

|                         | Radium only    | Combined treatment |
|-------------------------|----------------|--------------------|
| Inoperable cases .....  | 62.6 per cent. | 64.3 per cent.     |
| Border-line cases ..... | 6.6 per cent.  | 8.3 per cent.      |
| Operable cases .....    | 30.8 per cent. | 27.3 per cent.     |

The series of cases subjected to combined treatment include a slightly larger number of advanced cases than that in which radium only has been

used. In spite of this, however, the end-result with the combined treatment is decidedly better. From this one might feel justified in concluding that the combined treatment is superior to radium alone.

Against this, however, it might be rightly argued that the number of cases in the two series is not sufficiently large. It is quite conceivable of course that chance coincidences of different kinds, *e.g.*, some intercurrent deaths or cases where it has been impossible for some reason or other to carry through the treatment rationally, may make the result in the series of cases treated solely with radium appear worse than in the series subjected to the combined treatment.

It has seemed to me appropriate, therefore, to find out what the outcome would be of a comparison between larger series of cases.

If the apparently better end-result of the combined treatment is really due to the parametric Röntgen irradiation, then the end-result during 1918-1920 inclusive, when the combined treatment was that mainly employed, ought to be better than the average result during the other years.

I have therefore compared the results from the period 1918-1920 inclusive during which time the combined treatment, as will be clear from Table I, was used in 66.2 per cent. of cases, with the result obtained in the total number of 737 cases treated during the ten-year period 1914-1923. It is true that during all these ten years the radium treatment has not been carried out in so strictly uniform a manner as during the period mentioned above and, further, that this series also includes the cases treated by Röntgen. However, the errors occasioned by these two factors are likely to outweigh one another. Also such chance coincidences as mentioned above may be considered eliminated in this relatively large series.

This comparison shows:

|                           |                                 |
|---------------------------|---------------------------------|
| 1914-1918 inclusive ..... | 23.1 per cent. five-year cures. |
| 1914-1920 inclusive ..... | 26.8 per cent. five year cures. |

During these two periods the cases were divided as follows:

|                         | 1914-1923      | 1918-1920      |
|-------------------------|----------------|----------------|
| Inoperable cases .....  | 66.8 per cent. | 66.7 per cent. |
| Border-line cases ..... | 7.7 per cent.  | 8.5 per cent.  |
| Operable cases .....    | 25.5 per cent. | 24.9 per cent. |

It will be seen, therefore, that the initial material is almost identically the same.

This comparison, too, is in favor of the combined treatment. Our original opinion of the value of the parametric Röntgen irradiation, based on the primary results obtained, can no longer, therefore, be maintained. No other conclusion can apparently be drawn from my investigation than that the combined treatment has brought with it a more favorable end-result than intragenital treatment by radium alone.

It is to be noted, however, that the superiority of the combined treatment is by no means so obvious as has been suggested in some quarters.

## TREATMENT OF CANCER OF CERVIX UTERI

There is no doubt whatever that radium irradiation is by far the more important part of the treatment.

In my statistical examinations I have also tried to find an answer to two more questions:

Firstly, whether the parametric irradiation has improved the result in all the various stages of cervical carcinoma.

And secondly, whether any one particular variation in the Röntgen technic employed has yielded better results than any other.

With regard to the first of these questions it is of interest to find out whether the demonstrated superiority of the combined treatment is equally obvious in the operable as in the inoperable cases.

As in the group of operable cases no involvement of the parametria is clinically obvious, it might seem as if irradiation of the parametria would be unnecessary in these cases.

In the subjoined tables I have compared the result of the combined treatment, on the one hand, with the average result from the whole period, 1914-1923, when radium was the treatment mainly used and, on the other hand, with the result of radium treatment alone during the period 1918-1922.

In so doing I have included the operable and inoperable cases but left out the few border-line cases, for during the period 1918-1922 these numbered only thirty-three while the inoperable cases numbered 289 and operable 135.

The distribution of cases in the three series (border-line cases excluded) will be clear from the following table:

TABLE I

|               | All cases<br>1914-1923 |       | Treated by<br>radium only<br>1918-1922 |       | Combined treatment<br>1918-1922 |       |
|---------------|------------------------|-------|--|-------|---------------------------------|-------|
|               | Number of<br>cases     | Cured | Number of<br>cases                     | Cured | Number of<br>cases              | Cured |
| Inoperable... | 492                    | 64    | 181                                    | 17    | 108                             | 19    |
| Operable..... | 188                    | 82    | 89                                     | 37    | 46                              | 24    |

I give this table only to show the number of cases within the different groups. As will be noticed, especially in the operable cases, the primary figures, on which the cure rate in the following table has been calculated, are small, thus reducing to some extent their proof value.

TABLE II

*The Cure Result in Inoperable and Operable Cases with Combined Treatment Compared with the Average Result 1914-1923 and the Result of Radium Treatment Alone During 1918-1922*

|                 | All cases<br>1914-1923 | Radium only<br>1918-1922 | Combined<br>treatment<br>1918-1922 |
|-----------------|------------------------|--------------------------|------------------------------------|
| Cure rate       |                        |                          |                                    |
| Inoperable..... | 13.0                   | 9.4                      | 17.6                               |
| Operable.....   | 43.6                   | 42.8                     | 52.1                               |

Table II shows that the combined treatment gives better results, both in inoperable and in operable cases. This fact is more marked in the inoperable series, although a not inconsiderable improvement is noted also among the operable cases. It would seem justifiable to conclude from the relatively large number of inoperable cases, and the considerable improvement of the results in this group, that the combined treatment of inoperable cases is superior to radium treatment alone. With regard to operable cases it seems doubtful whether any conclusion can be drawn. It is perhaps more prudent to wait until a larger series of cases which have been subjected to the combined treatment is available.

The technical procedure in applying the Röntgen treatment during these therapeutic attempts has varied in several respects. These variations refer in the main to the number of entrance fields, the number of irradiations and their distribution in series, the interval between the series, and lastly, the time of application of the Röntgen in relation to the radium treatment. I am going to deal only with the last of these factors. With regard to the other factors, it is not possible to divide the available material into groups large enough to allow conclusions to be drawn.

In one series, the larger one, the Röntgen treatment has been given during the three weeks that, according to our standard technic, are allowed to elapse between the second and the third radium application. This form of treatment has been designated Rö. III in our tables. In a smaller series of cases the Röntgen treatment was started after the third radium application, not later than one month after, usually within fourteen days (Rö. II).

TABLE III

*Combined Treatment. Röntgen Treatment After the Third Radium Application (Rö. II)*

|                           | Number of<br>cases | Cured<br>(5 years) | Cure rate     |
|---------------------------|--------------------|--------------------|---------------|
| All cases.....            | 53                 | 17                 | 32.1 per cent |
| Of which: inoperable..... | 39                 | 9                  | 23.1 per cent |
| border-line.....          | 4                  | 2                  | 50.0 per cent |
| operable.....             | 10                 | 6                  | 60.0 per cent |

We have also tried to start with Röntgen treatment and to give the radium subsequently (Rö IV). On account of various circumstances these cases have been relatively few in number and will not be included in what follows.

In Table III and Table IV the figures referring to the two series above mentioned are submitted.

TABLE IV

*Combined Treatment. Röntgen Treatment Between the Second and Third Radium Application (Rö. III)*

|                           | Number of<br>cases | Cured<br>(5 years) | Cure rate     |
|---------------------------|--------------------|--------------------|---------------|
| All cases.....            | 115                | 32                 | 27.9 per cent |
| Of which: inoperable..... | 69                 | 10                 | 14.5 per cent |
| border-line.....          | 10                 | 4                  | 40.0 per cent |
| operable.....             | 36                 | 18                 | 50.0 per cent |

## TREATMENT OF CANCER OF CERVIX UTERI

The results in the two series have been compared in Table V.

TABLE V

*Comparison Between the Cure Results in Rø. II and Rø. III*

|                  | Rø. II        | Rø. III       |
|------------------|---------------|---------------|
| All cases.....   | 32.1 per cent | 27.9 per cent |
| Inoperable.....  | 23.1 per cent | 14.5 per cent |
| Border-line..... | 50.0 per cent | 40.0 per cent |
| Operable.....    | 60.0 per cent | 50.0 per cent |

It will be clear from the comparison made in Table V that the end-result throughout is somewhat better in the first group (Rø. II) than in the latter.

True that the border-line and operable cases are few in number, and the relatively slight difference as regards the cure result may conceivably be due to some chance coincidence. On the other hand, the difference in the cure rate in the comparatively large group of inoperable cases is sufficiently well marked to show that the form of combined radium-Röntgen treatment where the Röntgen is given after the completed radium treatment is to be preferred.

Our experiences have led us to combine, since 1929, our radium treatment with Röntgen irradiation of the parametria as a routine, at least in inoperable cases, and to start the Röntgen treatment within a month of the final radium application.

These attempts with combined radium-Röntgen treatment were commenced simultaneously with the introduction of the deep Röntgen therapy at Radiumhemmet. Our therapeutic technic has developed with the rapid improvement in technical resources during these years and has gradually become modified according to experience gained. It is beyond the scope of this investigation to relate in detail how this technic has varied. The majority of cases has been treated on fairly uniform lines as far as the more important factors in the technic are concerned.

The following conditions prevailed in most cases during the period 1918-1922: Inductor coil with gas tube (S.H.S.). Peak voltage, 160-180. Milliamperage 2-2.5 milliamperes. Filter: during 1918, 4 millimetres aluminum, from 1919 inclusive 0.5 millimetre copper + 1 millimetre aluminum. Skin-focus distance: at first 20 centimetres later generally 30 centimetres.

In all cases two abdominal fields were used, in nearly all of them in addition two posterior fields and occasionally also a perineal field were used. The fields have nearly always been rectangular, varying between 10 and 13 square centimetres. The depth dose at 10 centimetres depth and at a skin-focus distance of 20-30 centimetres is estimated as 20-25 per cent. of the skin dose.

*Dosage.*—During the years under review the dose was measured at Radiumhemmet by Holzknecht's units and tablets. According to statistical data pertaining to the Röntgen dosage in Sweden (Sievert: *Acta Radiologica*, vol. vii, p. 401) one S.U.D. approximately corresponds to fifteen to sixteen Holzknecht units. With the radiation intensity attained at that time it may

be assumed that one S.U.D. with 4 millimetres aluminum corresponded to about 600 Behnken's units and with 0.5 millimetre copper + 1 millimetre aluminum to about 700 Behnken's units.

The skin dose at each application was: ten Holzknecht units, occasionally fifteen Holzknecht units, exceptionally five Holzknecht units.

The number of fields in each series of treatments was usually four, two anterior and two posterior. Only one application was given daily. A series consisted of one application to each field, in all four applications the fields being irradiated in rotation. Usually two series were given consecutively, each field thus generally receiving a total of twenty Holzknecht units. Some of the earlier cases received three series consecutively. Subsequent experience regarding the local as well as general reaction of the patients caused us, however, to interpose an interval of one or several months between the second and third series.

In cases proceeding favorably it gradually became the rule not to repeat the treatment after the conclusion of two series. With the more powerful apparatus that came into use later and the consequently much increased radiation intensity, we deemed it appropriate to reduce not only the single dose but also the aggregate dose per field and further to reduce the number of irradiated fields.

Since 1929 the following technic has been in use:

Transformer with valve-tubes and condensers. Coolidge tube. Constant voltage 160-170. Milliamperage: 6 milliamperes. Filter: Thoriaeus' tin-filter equivalent to three millimetres copper (*Abstracts of Communications*, Second Radiological Congress, 1928). Skin-focus distance: 30-40 centimetres according to the thickness of the abdominal wall. No compression.

Entrance fields: Two abdominal, 10 to 13 square centimetres. Beam centered on the subjacent parametrium.

Each field receives 3 by  $\frac{1}{4}$  S.U.D. Only one field is irradiated per day, left and right alternately. If the patient's general condition is appreciably affected the treatment is stopped for a day or two; as a rule, however, the Röntgen treatment can be carried out in the course of six consecutive days. In advanced cases or in cases where the radium treatment does not seem to be yielding the expected result, it may be necessary to give a larger Röntgen dose. This can be done by irradiating two posterior fields provided the patient's general condition and blood picture remain good. All patients are kept under careful observation and as long as they are progressing favorably the treatment is not repeated.

For the time being this method of irradiating the parametria will form a routine part of our treatment for inoperable carcinoma of the cervix. Until we have gained sufficient experience most operable cases will be similarly treated.

To what extent treatment by Röntgen may be replaced in the future by treatment by radium at a distance will depend upon the outcome of experiments which we have recently started.

# TREATMENT OF CARCINOMA OF THE CERVIX UTERI.

BY WILLIAM P. HEALY, M.D.

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HAS the question of treatment for carcinoma of the cervix uteri been settled? If not, what are the chief differences of opinion and the reasons therefor?

Briefly, it may be said that, previous to the discovery of radium and the subsequent recognition of its therapeutic qualities in the treatment of cancer, the only methods of treatment in vogue for cancer of the uterine cervix were those dependent upon surgical procedures. There were cautery operations, such as the high amputation of the diseased cervix with the actual cautery, as advocated and practiced by Byrne, or the slow, complete destruction of the growth by the prolonged application of heat with a hot soldering-iron, according to the method of Percy. There was the operative removal of the entire uterus with its adnexæ and the adjoining parametrial connective tissues and lymphatics by vaginal route (Schauta) or by the abdominal route (Wertheim).

There was also a combination of cautery and surgical treatment in which the cervical lesion was first thoroughly destroyed by heat and then the hysterectomy was done either at once or shortly after.

The success attending any one of the procedures mentioned varied with different operators, but, on the whole, the problem was most discouraging as the cures were so few and the failures so many.

The chief obstacle to success was the same then as it is today—the disease had become too extensive before it was recognized.

The absence of symptoms which would enable the physician to recognize the disease while it was still localized at its original site and before it had spread to adjoining structures and neighboring lymph-glands accounted for the high percentage of advanced and therefore incurable cases.

Nevertheless, specialists in pelvic surgery attacked this discouraging situation with courage and resourcefulness and finally the splendid operative procedure known as the Wertheim abdominal hysterectomy was developed and perfected in 1898.

Fundamentally, this consists not only in the removal of the uterus and adnexæ, but also the clearing out of all the parametrial connective tissues, lymphatics and regional lymph-glands and the amputation with the uterus of the upper third of the vaginal tube. This operation required the recognition and exposure of both ureters throughout the greater portion of their pelvic course and it interfered greatly with the support and innervation of the bladder. It was an extremely tedious and, indeed, difficult surgical procedure. The result was a high primary operative mortality which was entirely out of proportion to the benefit to be expected for those that survived. This



was not to be wondered at when it was realized that 40 to 60 per cent. of the cases in which operation was attempted had already developed regional lymph-gland metastases.

A study of gynecologic literature from 1900 to 1920 will show that earnest and conscientious efforts were made by competent surgeons to cure carcinoma of the cervix by means of the Wertheim hysterectomy and that the end-results were far from satisfactory to the surgeon.

There is no doubt, however, that this procedure increased the operability rate so that many more cases were subjected to major surgery under this plan than previously. In fact, Bonney thinks the operability rate increased to 50 per cent. or more. Bonney is probably the outstanding exponent today of the Wertheim plan of treatment for carcinoma of the cervix. He is a surgeon of unusual skill and judgment, he has earnestly and conscientiously applied himself to the development of a technic which would permit him to obtain the best possible results by surgical methods, and he has been able to reduce the primary mortality in his last five-year series to 16.5 per cent.

BONNEY did his first Wertheim in 1907. In the twenty-three years from 1907 to 1929, inclusive, he did the operation 382 times. He thinks his operability rate is 63 per cent. or more, so that during those twenty-three years he saw about 450 cases. This would leave a very large number of cases of carcinoma of the cervix in England available for operation during those years by other surgeons, but very few reports are available.

Bonney gives two reasons in explanation for the extremely small number of papers from surgeons dealing with a large series of Wertheim operations. Both reasons seem inadequate and fail to explain. It would seem more probable that surgeons have no large series of Wertheim operations to report, as they have, after giving it a fair trial, been discouraged and therefore discarded the operation as a routine treatment for carcinoma of the cervix for good and sufficient surgical reasons. These reasons have been stated many times in the past twenty-five years and are also emphasized in Bonney's Hunterian Lecture. They are, briefly, the distressing post-operative sequelæ in the form of sepsis, ureteral, vesical and intestinal fistulæ, long period of invalidism, and high primary mortality.

These unfortunate and serious complications may be expected with confidence since they occur in the practice of all surgeons who attempt the operation, even the most expert, including Bonney himself. Under those circumstances, surgeons and gynecologists of recognized skill and experience who have, with patience and great courage, attempted to cure carcinoma of the cervix with the Wertheim operation, have given it up as an unjustifiable routine surgical procedure.

Bonney's five-year statistics—284 operations to the end of 1924—show a primary mortality of 16.5 per cent. and a cure rate of 28.7 per cent.

With the discovery of radium and the advent of radiation therapy in the treatment of cancer, it was a natural sequence that methods were devised looking toward control and cure of carcinoma of the uterine cervix by radiation therapy.

In Europe, Regaud, Forssell, Heyman, Döderlein, and in the United States, Kelly, Burnam, Schmitz, John Clark, Bailey—all were pioneers in developing various plans of attack upon the disease and different methods of radiation therapy.

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The anatomical location of the cervix, its accessibility and the presence of the cervical canal, permitting attack from within as well as without and the fact that the cervix had no vital function to perform—all tended to create a situation favorable for study and treatment of the disease.

Finally, from the various clinics under control of the investigators named, as well as from other clinics, reports favorable to radiation therapy began to appear. As was to be expected, at first these reports dealt only with the treatment of advanced or inoperable cases, as the favorable cases still were subjected to operation.

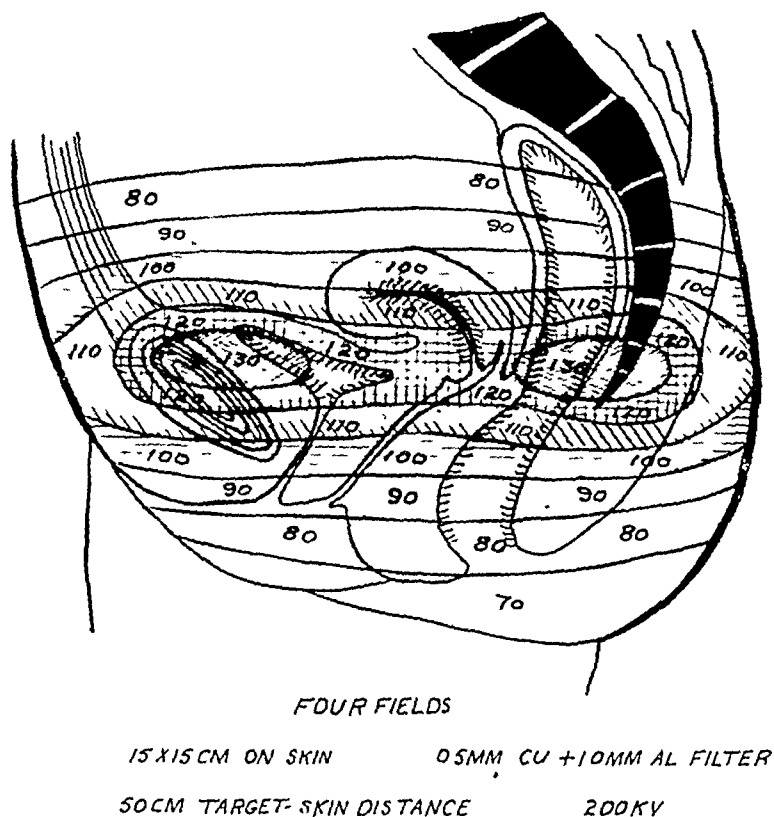


FIG. 1.—Sagittal section of average female pelvis. Showing distribution of radiation from X-ray pelvic cycle—four fields—15 by 15 centimetres on skin, 200 kilovolts, 0.5 millimetres copper and 1 millimetre aluminum filter, 50 centimetres target-skin distance. One erythema dose to each area.

The palliative results were so surprisingly satisfactory that inevitably less and less advanced cases were accepted for such treatment. Finally, because of the good results obtained with them and the absence of primary mortality and serious complications, even the early and most favorable cases were subjected in many clinics to radiation therapy instead of operation.

Radiation therapy has been, no doubt, somewhat handicapped because of the great cost of radium. Nevertheless, enough of the element has been available in different institutions in Europe and America since 1915 to permit large series of cases of carcinoma of the cervix to be treated with radium alone or in combination with Röntgen-ray. Papers dealing with the ex-

perience of the surgeons in these institutions have been published from time to time and we now have available for study a rather voluminous literature from all over the world covering the treatment of cases with radiation therapy only, the number of which now reaches into the thousands.

Incidentally, the establishment of radiation therapy has also placed upon a firm basis the importance and necessity of an accurate follow-up clinic, and has emphasized the value of a well-organized social service department for keeping in touch with the patients, especially of the poorer financial class.

As experience in the radiation therapy of carcinoma of the cervix has accumulated, it has been realized that a large amount of radium is not essential in the treatment of an individual case, but that 150 milligrams of the element disposed in needles and capsules of different strengths, thus permitting them to be used in applicators of various shapes and sizes, are quite sufficient for thorough treatment of any case of carcinoma of the cervix, especially if it can be combined with deep Röntgen-ray therapy by means of the high-voltage machine.

This is important from the economic standpoint, as it permits the treatment to be carried out by physicians or medical groups in many centres of population instead of restricting it to large institutions.

Nevertheless, it may here be quite properly pointed out that the large institution or hospital devoted exclusively to the study and treatment of cancer and allied diseases has a most important function to perform from the standpoint of research and education as well as treatment.

Such institutions, with their large laboratories and staffs of trained specialists, not only elucidate obscure problems and develop new methods of technic, but offer to the medical profession facilities for advanced study as internes and as post-graduate students.

From Radiumhemmet, in Stockholm, there have been a number of interesting and valuable reports by Forssell and Heyman concerning their experience with radiation therapy in carcinoma of the cervix.

HEYMAN, in a study of 3,184 cases of cancer of the cervix uteri, radiologically treated, collected from thirteen clinics, concluded that permanent healing for a period of five years or more may now be counted on with the technic generally employed in about 16 or 17 per cent. of the total number of applicants.

The absolute healing percentage obtained at Radiumhemmet in 500 cases was 22.4 per cent. for five years or more.

Heyman emphasizes the important difference in the character of the material dealt with in computing end-results in cases treated surgically or by radiation therapy.

The surgical statistics nearly always deal with series of cases of high operability, usually 50 to 60 per cent. of the cases being regarded as operable, whereas the operability percentages in cases treated by radiation therapy are, in the majority of instances, less than 30 per cent.

Heyman concludes from a study of surgical and radiation percentages as to end-results in different clinics throughout the world that primary healing obtained by radiation therapy is just as permanent as is surgical healing. This is important.

Results at Radiumhemmet depend almost exclusively upon the use of radium alone

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without X-ray or operation. As to the treatments, two or three in number are given in the course of a short time, at most from three to four weeks.

The last report from Radiumhemmet gives the following five-year end-results: Absolute cure rate in the treatment of carcinoma of the cervix, 20.6 per cent.; cure rate in operable cases of carcinoma of the cervix, radiologically treated, 40.4 per cent.

It is now fully established that the most important factor controlling the permanence of cure, regardless of the method of treatment employed, is the clinical or gross extent of the disease when treatment is begun. Thus, early diagnosis establishes ground for a good prognosis in 60 per cent. of the cases.

In addition, however, a study of end-results obtained in cases treated by radium alone or in combination with X-ray has led to the conclusion by some investigators (Healy and Cutler) that the histological structure of the

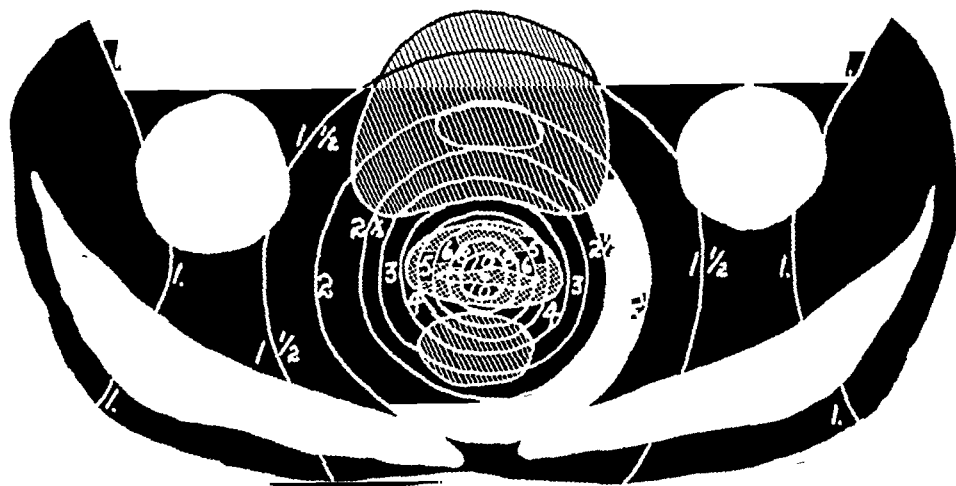


FIG. 2.—Tissue doses delivered throughout the average female pelvis by radiation given as follows: (1) Vaginal bomb=3 positions, 1000 millicurie-hours in each; (2) intra-uterine tandem=1000 millicurie-hours from upper tube, 2000 millicurie-hours from lower; (3) X-rays.—High voltage pelvic cycle, four fields, 1 skin erythema dose on each. Stated in terms of skin-erythema dose. (One-fourth life-size.)

tumor has a decided bearing upon prognosis, especially in advanced cases, when radiation therapy is the method of treatment employed.

For a long time, it was felt that the difference noticed in the response of cases of cancer of the cervix to radiation therapy could be explained in various ways but finally it was recognized that many of the tumors must be regarded as being especially radiosensitive judging by their rapid and oftentimes complete disappearance after treatment.

About 96 per cent. of all cases of cervical cancer belong histologically in the squamous epidermoid cancer-cell group. The remainder are classified as adenocarcinoma.

The tumors which seem to be most radiosensitive are those in which the histological structure is of the embryonal or immature cell type with marked evidences of anaplasia and little stroma. These, it is also interesting to note, are regarded histologically as the most malignant.

Possibly 17 to 20 per cent. of all cases of cervical cancer are in the very radiosensitive group.

The sensitivity to radiation seems to diminish as the cell type becomes more mature and more like the fully developed adult squamous cell.

This is the most resistant cell type to radiation therapy in the cervix and includes about 20 per cent. of all cases. The remaining 60 per cent. of cases between the two groups referred to may vary in response to radiation therapy

according to the proportion of the two types of cells, embryonal or adult, present, or of cells resembling or approaching one or the other group in histological characteristics.

That these two factors, early diagnosis and histological structure of the tumor, are not the only important factors influencing end-results is indicated by the large number of apparently favorable cases that die (25 to 40 per cent.) within five years after treatment, even when this has been promptly instituted.

It would appear from the high percentage of fatalities resulting from recurrence of cancer in the early or operable group within five years of the treatment, whether radiological or surgical,

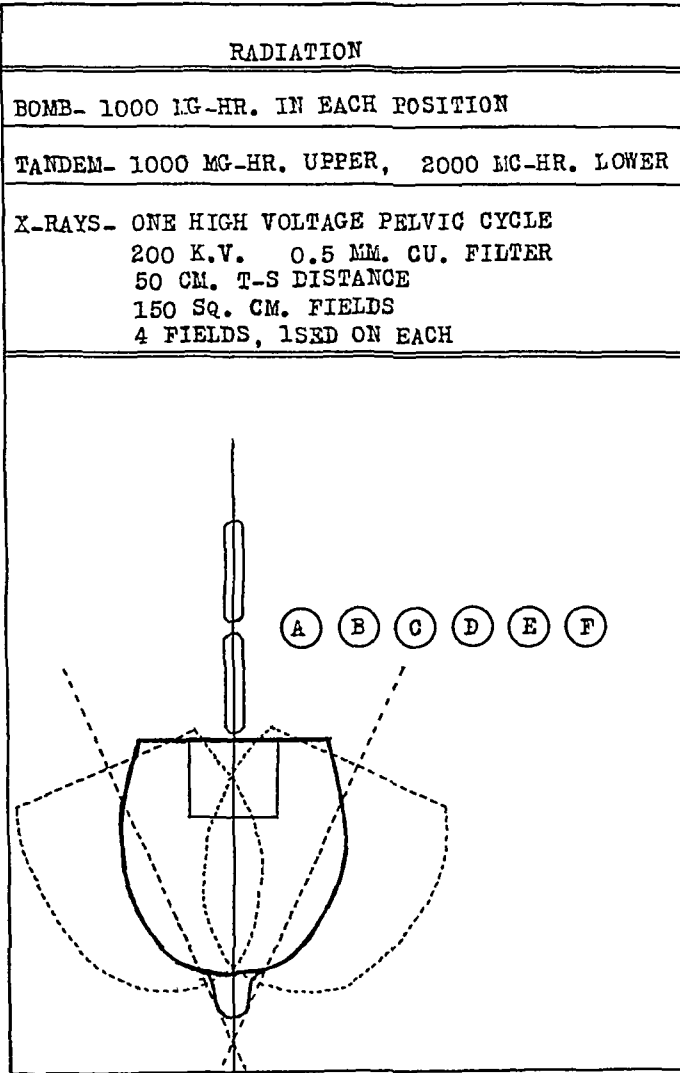


FIG. 3

that we cannot be satisfied with our present method of treatment.

These fatalities seem to be due to metastases which have occurred early in the course of the disease but which have eluded the surgeon's knife or have resisted the action of radium and X-ray, despite the fact that such metastases must be extremely small in order not to be recognized.

In the majority of instances, the recurrences are in the lymphatic glands of the broad ligaments or in the presacral and prevertebral lymphatic glands.

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At times the recurrence is situated in the cellular tissues surrounding the outer end of the vaginal canal, just within the hymen.

Recurrences located about the vaginal vault or along the vaginal canal after hysterectomy are often amenable to radiation therapy. In Bailey's series, 1918 to 1921, 139 cases were treated with radium alone for post-operative recurrences and sixteen cases, or 11.5 per cent., remained well for six to nine years.

On the other hand, in our experience, retreatments for local recurrences after full radiation therapy for the primary lesion do not seem to be satisfactory. This is also the opinion of Heyman.

In 1924, there were 150 cases of primary carcinoma of the cervix treated at the Memorial Hospital.

TABLE I  
*Cases of Carcinoma of Cervix, 1924*

|                   |     | Alive 1930 | Per cent. Alive |
|-------------------|-----|------------|-----------------|
| Early .....       | 19  | 11         | 58              |
| Border-line ..... | 23  | 6          | 26              |
| Advanced .....    | 91  | 13         | 14.3            |
| Palliative .....  | 17  | 0          |                 |
|                   | —   | —          |                 |
| Totals .....      | 150 | 30         |                 |

TABLE II  
*Absolute Cure Rate in Cases of Carcinoma of Cervix Treated in 1924*

|   |                |
|---|----------------|
| Cases Treated .....                     | 150            |
| Cases Cured .....                       | 30             |
| Absolute Cure Rate .....                | 20 per cent.   |
| Absolute Cure Rate (Radiumhemmet) ..... | 20.6 per cent. |

TABLE III  
*The Cure Rate in the Operable Cases of Carcinoma of the Cervix Treated in 1924*

|                                       |      |
|---------------------------------------|------|
| Cases Treated .....                   | 42   |
| Cases Cured .....                     | 17   |
| Percentage Cured .....                | 40.5 |
| Percentage Cured (Radiumhemmet) ..... | 40.4 |

It will be seen from Tables II and III that the end-results obtained at the Memorial Hospital and the Radiumhemmet with regard to cures are alike.

As the attitude in each of these institutions is to treat all cases that apply, even if only for temporary palliation—and, in fact, very few cases are denied treatment—it is reasonable to assume that these statistics represent the best that may be obtained with our present methods of radiation therapy.

They will vary slightly from year to year, but, on the whole, they may be expected to remain stationary.

It would seem, then, that the outlook for cure of carcinoma of the cervix cases is not a happy one as a study of the leading surgical and radiation

statistics indicates that by either method of treatment 80 per cent. of all cases seen will fail to survive five years.

It is recognized that an individual surgeon or radiation therapist may, by special ability or technic, obtain somewhat better end-results than the average. This does not, however, alter the seriousness of the problem, which, after all, must be met by physicians of average ability and resources.

| TISSUE DOSES AT INDICATED POINTS |              |       |         |       |              |       |         |
|----------------------------------|--------------|-------|---------|-------|--------------|-------|---------|
| POINT                            | APPLICATOR   | % SED | % TOTAL | POINT | APPLICATOR   | % SED | % TOTAL |
| A                                | BOMB - LEFT  | 15    | 2       | D     | BOMB - LEFT  | 5     | 2       |
|                                  | " CENTER     | 70    | 7       |       | " CENTER     | 15    | 5       |
|                                  | " RIGHT      | 50    | 5       |       | " RIGHT      | 40    | 15      |
|                                  | TANDEM-UPPER | 235   | 25      |       | TANDEM-UPPER | 40    | 15      |
|                                  | " LOWER      | 470   | 50      |       | " LOWER      | 80    | 29      |
|                                  | X-RAYS       | 100   | 10      |       | X-RAYS       | 100   | 35      |
|                                  | TOTAL        | 940   | 100     |       | TOTAL        | 280   | 100     |
| B                                | BOMB - LEFT  | 10    | 2       | E     | BOMB - LEFT  | 5     | 2       |
|                                  | " CENTER     | 40    | 7       |       | " CENTER     | 10    | 4       |
|                                  | " RIGHT      | 60    | 10      |       | " RIGHT      | 30    | 13      |
|                                  | TANDEM-UPPER | 120   | 21      |       | TANDEM-UPPER | 30    | 13      |
|                                  | " LOWER      | 240   | 42      |       | " LOWER      | 60    | 26      |
|                                  | X-RAYS       | 100   | 18      |       | X-RAYS       | 100   | 42      |
|                                  | TOTAL        | 570   | 100     |       | TOTAL        | 235   | 100     |
| C                                | BOMB - LEFT  | 10    | 2       | F     | BOMB - LEFT  | 5     | 2       |
|                                  | " CENTER     | 25    | 6       |       | " CENTER     | 5     | 2       |
|                                  | " RIGHT      | 55    | 14      |       | " RIGHT      | 20    | 10      |
|                                  | TANDEM-UPPER | 70    | 17      |       | TANDEM-UPPER | 25    | 12      |
|                                  | " LOWER      | 140   | 35      |       | " LOWER      | 50    | 25      |
|                                  | X-RAYS       | 100   | 25      |       | X-RAYS       | 100   | 49      |
|                                  | TOTAL        | 400   | 100     |       | TOTAL        | 205   | 100     |

TABLE IV

The fact remains that only twenty cases out of every 100 are salvaged for five years.

On the whole, the most important fact is the necessity for early diagnosis, as 60 per cent. or more of the early cases may be expected to survive five years.

In the final analysis, then, it would seem that the skillful surgeon, qualified by special training and experience, may obtain in the operable cases as many cures as the skilled radiation therapist, but the surgeon will always

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have to combat a primary mortality much higher than that of radiation therapy, and also a much greater morbidity.

Two-thirds of the cases are not amenable to surgery and are treated best by radiation.

There are always twice as many cases, therefore, for radiation than for operation and as a result radiation therapists gain twice as much experience.

It is safe to say that today, despite the short time elapsed since the development of radiation therapy, there are more specialists qualified to treat carcinoma of the cervix properly with radium and X-ray than there are surgeons qualified to do a radical Wertheim hysterectomy.

This is in no wise a criticism of surgeons but is a natural outgrowth from a discouraging situation.

Radiation technic in the treatment of carcinoma of the cervix has made rapid strides and is no longer a hit-or-miss affair. The dosage to be obtained in different parts of the lesion and the pelvis can be determined with reasonable accuracy and the minimum amount of radiation necessary to take care of the lesion, measured in skin erythema doses, is fairly well known.

Fig. 1 indicates, in diagrammatic form, the distribution of radiation in an average female pelvis, from high voltage X-ray measured in skin erythema doses.

Fig. 2 indicates the total tissue doses delivered throughout the average female pelvis by combined radiation with radium applied directly to the lesion by means of vaginal and intra-uterine applicators and X-ray through four fields about the pelvis. The tissue doses are stated in terms of skin erythema dose.

Fig. 3 shows vaginal bomb applicator and intra-uterine radium tandem in position (actual size, diagrammatic).

See Table IV for doses delivered at lettered points two centimetres above external os and one to six centimetres distant from cervical canal.

In conclusion, it may be said that radiation therapy has a wider field of usefulness in the treatment of carcinoma of the cervix than has hysterectomy, as it may be used to advantage in the treatment of all cases, favorable and unfavorable for a cure.

The end-results in the favorable cases are, on the whole, somewhat better with radiation.

There is little, if any, place for hysterectomy in the treatment of advanced cases.



# LES MÉTASTASES DES ÉPITHELIOMAS DU COL UTERIN LOCALEMENT GUÉRIS PAR RADIOTHÉRAPIE

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L'ÉPITHELIOMA du col utérin, abandonné à son évolution naturelle, aboutit à une terminaison fatale en peu d'années (2 à 3 en moyenne). La cause de la mort consiste ordinairement en une complication qui peut être: a) locale (hémorrhagie, infection) b) de voisinage (compression des urètres, envahissement de la vessie, du péritoine, de l'intestin); c) distante (métastases). Ce cancer suit donc les étapes classiques dans l'envahissement de l'organisme.

Les voies de la généralisation des épithéliomas du col ont été depuis longtemps et minutieusement étudiées. Il a été établi que la dissémination résultait rarement de l'irruption du néoplasme dans une veine. En revanche, l'envahissement des vaisseaux lymphatiques se produit précocement; les métastases sont l'aboutissant du cheminement progressif du cancer dans les voies lymphatiques: étape par étape, c'est-à-dire à travers les différents groupes ganglionnaires, les cellules cancéreuses atteignent la grande circulation par le canal thoracique. Habituellement, ce long circuit et les barrières ganglionnaires multiples retardent la généralisation; en outre, le siège profond de ces voies lymphatiques, la difficulté de leur exploration dissimulent pendant longtemps leur envahissement. Aussi la plupart des malades non traitées succombent-elles du fait des complications locales avant que la généralisation ait eu le temps de se manifester cliniquement. Mais l'autopsie révèle la fréquence des métastases latentes.

Dans la période que l'on peut appeler l'*ère chirurgicale* du cancer du col (qu'on peut faire débiter vers 1890 environ), de nombreuses et minutieuses recherches ont fait connaître en détails tous les embranchements du réseau lymphatique que sont susceptibles d'emprunter les cellules cancéreuses. La précocité de leur envahissement a été établie; il a été démontré, que dans une proportion importante des cancers considérés comme au début en raison de la limitation apparente des lésions, les ganglions régionaux étaient déjà pénétrés par des éléments néoplasiques.

L'*ère radiothérapique* de l'épithélioma du col, bien qu'encore récente, a déjà eu pour conséquence d'entraîner certaines modifications importantes dans la marche habituelle de ce cancer. C'est ainsi qu'à L'Institut du Radium de Paris, par exemple, trois étapes dans la technique radiothérapique des épithéliomas du col se sont succédées au cours de ces 10 dernières années; à chacune d'elles ont correspondu certains tableaux cliniques particuliers.

a) Les premiers résultats obtenus par l'emploi des radiations le furent au moyen de la curiethérapie: un foyer placé dans le fond du vagin ou dans

l'ulcération du col, amenait (dans un certain nombre de cas) la fonte des bourgeons néoplasiques et la cicatrisation des ulcérations. Mais, en ce qui concerne surtout les cancers étendus, ce blanchiment des lésions apparentes ne durait généralement que peu de semaines; après quoi se produisait une récurrence locale. En définitive, la thérapeutique avait temporairement enrayer la marche de la maladie sans en modifier sensiblement le mode d'évolution.

b) Puis, dans une deuxième étape, la technique de la curiethérapie intracavitaire fut considérablement améliorée. Ces perfectionnements consistaient en l'emploi de foyers de radium faibles mais aussi nombreux que possible et fortement filtrés, en leur disposition rationnelle dans toute la longueur du canal au niveau de l'utérus et dans des positions d'élection fixes au niveau du vagin, en l'allongement sur plusieurs jours de l'irradiation continue. Conséquemment à ces progrès techniques, la guérison des épithéliomas au stade 1 devint presque régulière. Dans la plupart de ceux au stade 2, et même dans certains cas inopérables, on obtint la disparition des lésions perceptibles à l'exploration. Mais l'observation prolongée de ces malades mit souvent en évidence une évolution clinique particulière. Après six, huit mois, un an, ou même après plusieurs années, ces patients, dont l'état général était redevenu excellent, accusaient des douleurs sciatiques dont l'accentuation progressive tendait à les rendre intolérables; d'autres fois, une constipation opiniâtre représentait le premier signe anormal. L'exploration vaginale confirmait la disparition totale des lésions cervicales, mais le toucher rectal mettait en évidence la présence d'une tumeur profonde, tantôt présacrée, tantôt plaquée contre la paroi latérale de la cavité pelvienne et correspondant à une masse ganglionnaire hypogastrique.

c) A partir de 1924, et plus généralement en 1925, le traitement des épithéliomas du col inopérables consista dans la combinaison de la curiethérapie intracavitaire avec une irradiation pelvienne transcutanée, soit par röntgenthérapie, soit par curiethérapie à distance. Le résultat fut une augmentation importante de la proportion des guérisons de malades inopérables. Mais en même temps, un autre mode clinique d'évolution de l'épithélioma du col utérin augmentait de fréquence: la généralisation métastatique. C'est cette forme clinique que je me propose de présenter ici avant d'en discuter le mécanisme.

## RÉSUMÉ DES OBSERVATIONS

OBS. 1° XIV A 34.—59 ans. Stade 2. *Épithélioma pavimenteux épidermoïde*. Traitement le 6 mai et le 9 octobre 1919 par curiethérapie intracavitaire (Ra interne). Guérison apparente pendant 3 ans. En 1922, douleurs abdominales; on constate la présence d'une petite tumeur lombaire prévertébrale: lent développement de cette masse au cours des années suivantes. En février 1925, il existe plusieurs autres tumeurs abdominales (épigastrique, iliaque). Persistance de la guérison locale. Mort en juillet 1926.

OBS. 2° XIV A 198.—42 ans. Stade 1. *Épithélioma embryonnaire avec ébauche d'évolution épidermoïde*. Traitement le 10 décembre 1920. (Ra interne). En avril 1922, douleurs dans la région hépatique; en juillet, développement d'une tumeur du foie. Persistance de la guérison locale. Mort le 20 décembre 1922.

OBS. 3° XIV A 241.—42 ans. Stade 1. *Épithélioma pavimenteux épidermoïde*. Traitement le 5 novembre 1921 (Ra interne). En février 1923, douleurs lombaires: pas de signes à l'exploration du vagin et du rectum. A la fin de mars surviennent des phénomènes cérébraux: torpeur progressive, coma et mort par métastase crânienne probable le 9 avril 1923.

OBS. 4° XIV A 270.—55 ans. Stade 3. *Épithélioma pavimenteux épidermoïde*. Traitement le 27 mai 1922 par röntgenthérapie et curiethérapie intracavitaire combinées (RX ÷ Ra interne). Guérison apparente pendant 3 ans. En juin 1925, apparition d'un ganglion sus-claviculaire gauche; présence d'une tumeur lombaire prévertébrale. A partir de juin 1926, signes de compression intestinale; apparition d'un ganglion axillaire gauche; crises d'épilepsie jacksonienne. Persistance de la guérison locale. Mort le 24 novembre 1926.

OBS. 5° XIV A 411.—59 ans. Stade 3. *Épithélioma pavimenteux épidermoïde*. Traitement le 28 janvier 1924 (RX ÷ Ra interne). Guérison apparente pendant 4 ans. En mai 1928, douleurs lombaires. A la fin de cette année, signes de métastases pulmonaires; persistance de la guérison locale. Mort le 10 janvier 1929.

OBS. 6° XIV A 432.—53 ans. Stade 4. *Épithélioma pavimenteux épidermoïde*. Traitement le 29 mars 1924 (RX ÷ Ra interne). Guérison apparente pendant 4 ans. En septembre 1928, douleurs abdominales. En octobre, se développe une tumeur épigastrique prévertébrale. Persistance de la guérison locale. Mort au début de l'année 1929.

OBS. 7° XIV A 525.—47 ans. Stade 2. *Épithélioma pavimenteux épidermoïde*. Traitement le 13 juin 1925 (RX ÷ Ra interne). En décembre 1925, douleurs abdominales: présence d'une tumeur de la fosse iliaque gauche. En février 1926, développement d'une tumeur lombaire prévertébrale. Persistance de la guérison locale. Mort le 24 avril 1926.

OBS. 8° XIV A 527.—46 ans. Stade 1. *Épithélioma non épidermoïde*. Traitement le 15 juin 1925: curiethérapie intracavitaire suivie d'hystérectomie. En juin 1926, douleurs lombaires: l'exploration du vagin et du rectum est négative. En février 1927, apparition d'un ganglion sus-claviculaire gauche; en octobre 1927, adénopathie cervicale droite: la palpation révèle la présence d'une masse lombaire prévertébrale. Mort le 19 octobre 1927.

OBS. 9° XIV A 531.—48 ans. Stade 3. *Épithélioma pavimenteux épidermoïde*. Traitement le 26 juin 1925 (RX ÷ Ra interne). En octobre 1925, apparition d'un ganglion sus-claviculaire gauche. Signes de métastases pulmonaires; persistance de la guérison locale. Mort le 4 avril 1926.

OBS. 10° XIV A 539.—57 ans. Stade 2. *Épithélioma de transition*.\* Traitement le 7 août 1925 par curiethérapie intracavitaire et curiethérapie transcutanée combinées (Ra interne ÷ Ra externe). Guérison apparente pendant 3 ans. En décembre 1928, signes de métastases pulmonaires; persistance de la guérison locale. Mort en avril 1929.

OBS. 11° XIV A 556.—53 ans. Stade 3. *Épithélioma de transition*. Traitement le 20 octobre 1925 (Ra interne ÷ RX). Guérison apparente pendant 5 mois. En mars 1926, on perçoit par palpation abdominale, une tumeur lombaire prévertébrale. En juin 1927, la tumeur abdominale s'est développée et donne des signes de compression intestinale. Développement d'une tumeur épigastrique. Persistance de la guérison locale. Mort le 21 juin 1927.

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\* J'entends par épithélioma de transition une variété d'épithélioma qui prend ordinairement son origine dans la région endocervicale, au niveau du passage de l'épithélium pavimenteux à l'épithélium cylindrique et où débouchent les glandes du col. Dans ces épithéliomas, on retrouve à la fois, mais avec un degré de prédominance variable, certains caractères d'évolution épidermoïde et d'autres de sécrétion de mucus.

## RADIOTHERAPY CANCER NECK OF UTERUS

OBS. 12° XIV A 574.—47 ans. Stade 4. *Épithélioma pavimenteux*. Traitement le 12 décembre 1925 (Ra interne ÷ RX). Guérison apparente pendant 3 ans. En janvier 1928, développement de tumeurs abdominales, une lombaire prévertébrale et une dans la fosse iliaque droite. Mort le 15 mars 1929.

OBS. 13° XIV A 660.—63 ans. Stade 2. *Épithélioma de transition*. Traitement le 23 octobre 1926 (Ra interne). En juillet 1927, signes de métastase hépatique. Persistance de la guérison locale. Mort en septembre 1927.

OBS. 14° XIV A 765.—48 ans. Stade 2. *Épithélioma de transition*. Traitement le 18 octobre 1927 (Ra interne ÷ Ra externe). Guérison apparente pendant un an et demi. En juillet 1929, douleurs abdominales; en août, apparition d'une petite tumeur métastatique dans la paroi abdominale, qui est extirpée chirurgicalement. En octobre 1929, au dernier examen: toux, amaigrissement, sans signes objectifs; persistance de la guérison locale.

OBS. 15° XIV A 774.—53 ans. Stade 2. *Épithélioma pavimenteux épidermoïde*. Traitement le 13 novembre 1927 (Ra interne ÷ Ra externe). Guérison apparente pendant un an et demi. En avril 1929, signes de métastases pulmonaires. Persistance de la guérison locale. Mort le 24 novembre 1929.

OBS. 16° XIV A 783.—46 ans. Stade 3. *Épithélioma pavimenteux épidermoïde*. Traitement le 30 novembre 1927 (Ra interne ÷ Ra externe). En janvier 1928, douleurs intercostales et dans le bras gauche. En avril 1928, la radiographie révèle une métastase dans la tête de l'humérus gauche. En juillet 1928, signes de métastase hépatique. Persistance de la guérison locale. Mort en septembre 1928.

OBS. 17° XIV A 796.—54 ans. Stade 3. *Épithélioma pavimenteux épidermoïde*. Traitement le 9 janvier 1928 (RX ÷ Ra interne). En août 1928, apparition de nodules cutanés multiples, puis signes de généralisation viscérale: amaigrissement, dyspnée, gros foie, ascite. Persistance de la guérison locale. Mort le 5 septembre 1928.

OBS. 18° XIV A 875.—28 ans. Stade 2. *Épithélioma de transition*. Traitement le 9 octobre 1928 (RX ÷ Ra interne). Apparition en août 1929 de douleurs dans le bras gauche. La radiographie met en évidence une métastase de l'extrémité supérieure de l'humérus. Au dernier examen (mars 1930), persistance de la guérison locale.

### DISCUSSION DES CAS

A ces observations manque le contrôle de l'autopsie dont la pratique eût certainement, dans la plupart des cas, révélé des localisations insoupçonnées et conduit à des conclusions plus positives quant au mécanisme de la production des métastases. Des données de la seule clinique, il semble toutefois qu'on puisse tirer quelques indications. *Le chemin des métastases*.—La métastase par pénétration directe dans la circulation sanguine existe, à n'en pas douter, en ce qui concerne l'épithélioma du col utérin. Il arrive qu'on rencontre, à l'examen des préparations histologiques, des figures d'envahissement d'un vaisseau incontestablement veineux. Mais elle apparaît très rare par comparaison avec les généralisations par voie lymphatique.

Les observations cliniques conduisent à admettre que, dans le plus grand nombre des cas, le néoplasme s'est propagé par la voie lymphatique. Tantôt les éléments cancéreux, se multipliant dans les ganglions abdominaux, ont déterminé le développement d'une tumeur lombaire ou épigastrique qui a attiré l'attention par des signes de compression. Tantôt ces barrières ganglionnaires ont été rapidement franchies et, alors que la localisation prévertébrale n'était pas encore tangible, survint, comme symptôme apparemment initial, une hypertrophie ganglionnaire sus-claviculaire. C'est le signe de

TROISIÈME. Cet auteur établit, en 1888, que tout cancer de la cavité abdominale peut se propager à distance aux ganglions sus-claviculaires gauches; et parmi les observations rapportées par lui figurent plusieurs cas d'épithélioma du col utérin. Il expliquait cet ensemencement rétrograde par la possibilité d'un reflux de la lymphe au niveau de la crosse du canal thoracique, par suite d'une augmentation de pression dans le système veineux. Dans une récente publication ROBERTS admet un tout autre mécanisme de l'envahissement des ganglions sus-claviculaires, axillaires et trachéo-bronchiques dans les cancers abdominaux (prostate et col utérin): l'obturation néoplasique de la voie lymphatique abdominale entraînerait la dérivation de la lymphe par une voie spinale postérieure, qui serait en communication directe avec les affluents collatéraux du canal thoracique. Quoi qu'il en soit, dans 3 cas, parmi les 18 observations précédentes (4-9-10), le premier signe de certitude de la généralisation a été effectivement une hypertrophie ganglionnaire sus-claviculaire gauche.

Il semble bien que les différentes localisations pulmonaires, osseuses, cérébrales et même hépatiques, représentent des manifestations plus ou moins tapageuses de l'essaimage, par la circulation sanguine, de cellules cancéreuses qui y ont été déversées, après que le processus cancéreux a cheminé lentement et à bas bruit dans l'intérieur du système lymphatique jusqu'à sa terminaison. Peut être aussi arrive-t-il que le crible ganglionnaire laisse passer les éléments néoplasiques sans ralentir leur marche sensiblement: on assiste alors à une généralisation d'emblée, comme cela semble avoir été dans le cas 17.

*Délai de production des métastases.*—Quel que soit le mécanisme de la dissémination des cellules cancéreuses, on est frappé par la longueur de la période de guérison apparente qui souvent fait suite au traitement et, par conséquent, par la lenteur d'évolution du processus néoplasique (4 ans dans les cas 5 et 6). Sans doute, il peut arriver qu'une tumeur ganglionnaire prévertébrale acquière un très gros volume sans donner de symptômes d'alarme et sans que, chez des femmes grasses, la palpation de l'abdomen permette de révéler leur présence. Mais, on ne peut que formuler des hypothèses sans fondement pour tenter d'expliquer, dans la plupart des cas, la longue quiétude des cellules malignes dans les métastases ganglionnaires alors que, au niveau du col, la progression du cancer semblait avoir subi son cours régulier.

L'examen histologique ne fournit pas d'indication à ce sujet; on trouve, parmi les cas ayant donné lieu à des métastases, des représentants de toutes les espèces d'épithéliomas habituellement rencontrés au niveau du col; cependant la proportion des épithéliomas pavimenteux épidermoïdes y dépasse de beaucoup le pourcentage ordinaire.

Contentons-nous donc d'enregistrer le fait clinique (qui n'est d'ailleurs pas particulier au cancer de l'utérus) de la grande inégalité d'évolution et du délai très variable de l'apparition des métastases. Par opposition avec la lenteur de la marche dont nous venons de parler, signalons, en effet, la possibilité d'une très rapide généralisation (cas 17). Il en fut ainsi égale-

ment chez une malade traitée par Ra interne en 1920 (obs. XIV A 193), dont nous avons préféré donner l'histoire résumée à part des précédentes observations. La lésion paraissait limitée au col (stade 1) ; cependant, au cours d'un examen pratiqué moins d'un mois après le traitement, on percevait déjà une masse abdominale lombaire ; 1 mois plus tard, apparaissait un ganglion sus-claviculaire gauche ; après 3 mois de plus, une tumeur épigastrique était signalée ; enfin des hémoptysies témoignaient du développement de métastases pulmonaires et la malade mourait 14 mois après le traitement.

Mêmes écarts considérables en ce qui concerne la survie des malades. Comparons à ce point de vue la malade de l'observation qui vient d'être rapportée à celles des cas 1, 5 et 6, qui ont survécu plus de 5 ans après leur radiothérapie.

Mais dans aucun cas, une métastase ne s'est démasquée au delà de 4 ans après le traitement, ce qui confirme la correction du délai de 5 années exigé par les conventions pour entériner la validité de la guérison d'un épithélioma du col utérin.

*Fréquence des métastases.*—On ne peut manquer de remarquer, non sans surprise au premier abord, que les généralisations, rarement observées parmi les malades traitées, dans les premières années, l'ont été ensuite avec une fréquence beaucoup plus grande. L'année 1925 marque à ce point de vue un fâcheux record. Il est à craindre que, parmi les malades traitées en 1926 et surtout en 1927 et 1928, considérées aujourd'hui comme guéries, d'autres cas de métastases se manifestent encore. La constatation d'une telle multiplication pourrait inciter à inculper la radiothérapie de provocation à la métastase ! Tout esprit judicieux écarte bientôt une telle supposition.

En réalité, la progression de l'incidence des métastases chez les malades localement guéries a suivi légitimement celle du nombre des malades guéries par les radiations. Ces guérisons sont devenues sans cesse plus fréquentes depuis 1919, grâce aux progrès considérables réalisés en technique radiothérapique. Rappelons, en effet, que la statistique de l'Institut du Radium de Paris, comprenant la totalité des épithéliomas du col traités par les radiations, indique un nombre de guérisons après 5 ans d'observation atteignant : 10 per cent. pour l'année 1919, 17 per cent. pour l'année 1920, 25 per cent. pour 1921, 26 per cent. pour l'année 1922, 30 per cent. pour l'année 1923, 35 per cent. pour 1924 ; on peut dès maintenant estimer que pour 1925, le nombre des guérisons après 5 ans atteindra 40 per cent.

Au reste, si la fréquence des métastases a augmenté, celles-ci frappent surtout des malades traitées pour des lésions beaucoup plus avancées ; dans les premières années, les quelques cas observés concernaient des malades atteintes de cancers au stade 1 ou 2, car la guérison locale des cas plus étendus n'était alors obtenue qu'exceptionnellement. L'accroissement brusque des métastases en 1925 correspond à l'époque où la combinaison systématique de l'irradiation externe transcutanée avec la curiethérapie intracavitaire pour le traitement des malades inopérables a permis de hausser les guérisons de ces cas à un taux jusqu'alors inconnu.

Il semble qu'on puisse expliquer par le même raisonnement pourquoi les cancers ayant donné lieu à des métastases appartenaient pour la plupart (surtout pendant les premières années) à l'espèce épithélioma pavimenteux épidermoïde: ce cancer étant le plus radiosensible des épithéliomas du col fournissait un plus grand nombre de guérisons locales.

#### CONCLUSIONS

L'étude des récidives extrapelviennes apporte donc une preuve de l'efficacité de la radiothérapie des épithéliomas du col utérin et des progrès réalisés depuis 10 ans dans cette voie. Elle montre que si par l'irradiation correcte du bassin, on peut obtenir la stérilisation d'un cancer propagé à toute la cavité pelvienne, lesensemencements extra-pelviens, préexistant au traitement, échappent évidemment à cette stérilisation. Les ganglions lombaires représentent le centre habituel de ces ensemencements d'où partiront ultérieurement, après une période de latence plus ou moins longue, les cellules génératrices des métastases. Comme la radiothérapie reste impuissante contre les cancers généralisés (l'irradiation des foyers métastatiques essayée plusieurs fois, bien que cela n'ait pas été rapporté dans les résumés ci-dessus, n'a pas empêché la terminaison fatale), il importe d'essayer de prévenir la généralisation. Pour cela, on cherchera à comprendre la région des ganglions lombaires dans le champ des irradiations chaque fois où l'extension des lésions pelviennes fera suspecter leur intégrité.

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# HOW FAR CAN RADIUM REPLACE RADICAL SURGERY FOR CANCER OF THE RECTUM

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IN THE treatment of cancer of the rectum radium has been employed for many years, chiefly as a palliative measure, and mainly by intrarectal application in cases regarded as unsuitable for radical surgery. It is only within the last six years that attempts have been made to use radium by interstitial needling in association with the surgery of access with a view to eradication of the disease. Great credit is due to Neumann, of Brussels, for his pioneer work in this direction. Most of the work done has been focused on cases regarded as inoperable or unsuitable for operation.

It is generally recognized that radical surgery for cancer of the rectum *in the early stage* cures a very high percentage of those who recover from the operation but it involves the stigma of colostomy.

It is accepted, in certain histological grades of cancer of the tongue, that radium can be relied on to produce as good, if not better, results (*quâ* the tongue) than mutilation by excision. The author has, in a limited number of cases, more especially when operation has been refused or considered undesirable on general grounds, attempted to find out if adenocarcinoma of the rectum can be placed on the same footing, and whether and under what circumstances it is justifiable to recommend radium in preference to radical excision and colostomy.

It is not proposed in this paper to discuss the value of radium treatment in those cases which have advanced so far that radical surgery is out of the question. Experience shows that much can be done for these and that a few can be relieved of all evidence of disease. The subject has been fully discussed by the author elsewhere.\*

It is proposed to consider here how far the use of radium is justifiable in preference to radical surgery. The problem is not only one of radiation *versus* colostomy and excision of the rectum but also radiation *versus* local resection without colostomy.

For many years partial resection of the rectum for an operable growth has been regarded as unsound surgery and has been replaced by some form of radical excision which is usually combined with colostomy.

The recent work of Dr. Cuthbert Dukes,† which, though subject to confirmation in a larger series of cases, shows on histological evidence that

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\* Radium Treatment of Cancer of the Rectum. *Acta Radiologica*, vol. x, Fasc. 4, No. 56; The Treatment of Carcinoma of the Rectum with Radium. *British Journal of Surgery*, vol. xvii, No. 68.

† *British Journal of Surgery*, vol. xvii, No. 68, 1930.



lymphatic invasion does not occur until the growth has penetrated through the longitudinal muscular coat of the bowel. These observations, based on a very complete histological examination of a hundred consecutive specimens of excised rectums, indicate that surgeons may in future be content with limited resections without permanent colostomy for the early mobile growth which has not commenced to ulcerate. In some instances ulceration occurs early, before the growth has involved by lateral spread the major portion of the circumference. Ulceration indicates downward spread and early penetration of the muscular coat, so that the actual size of the growth, if considered apart from its mobility, is not a sure test of suitability for local resection. The only clinical tests available are a small growth which has free mobility and shows absence of ulceration. The last three cases of this type have been dealt with by local resection; two with temporary colostomy, and one without. All three have been shown subsequently to belong to Class B. It should be mentioned that Class A are those very early cases which have

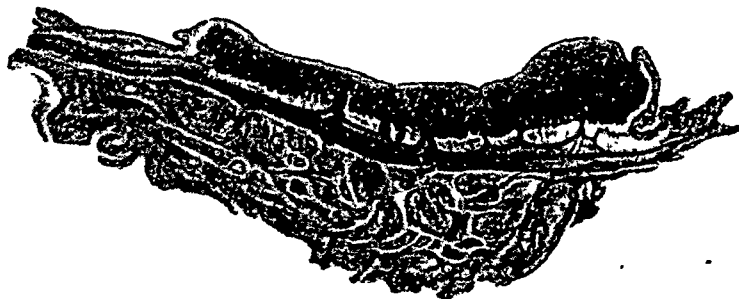


FIG. 1.—Carcinoma of the rectum, early C case. Longitudinal slice of the wall of the rectum, showing the manner in which a malignant growth invades the muscle coat by means of roots which push their way between the segments of the circular muscle.

not invaded the muscular coat, Class B, those which have invaded the muscular coat but not penetrated through it, and Class C, those which have penetrated the muscular coat and invaded the perirectal tissues. (Fig. 1.)

Time alone will show whether this procedure based on histological evidence is justified by ultimate results, though it may be mentioned here that the results of Harrison Cripps over twenty years ago, and Grey Turner in recent years, show that end-results of operations less radical than now considered necessary are remarkably good.

Can radium treatment compete with a local resection which aims at avoiding a permanent colostomy?

These three cases could have been dealt with quite easily and thoroughly by interstitial radiation. Two of them were amenable to vaginal radiation, and the other to a posterior barrage after resection of the coccyx. That these were not so treated, in spite of some successes in similar cases, is due to the fact that it was impossible to give any promise that radium would be

## RADIUM OR SURGERY FOR RECTAL CANCER

successful in completely destroying the growth and, if successful, that a recurrence was unlikely.

Sufficient evidence has been obtained to show that an early growth of the rectum can be destroyed with radium without colostomy (or with a temporary colostomy) and without interference with the function of the rectum, though no observations are available, on a five-year basis, as regards recurrence. If, however, local resection with little or no immediate mortality, carried out without permanent colostomy, should replace radical excision for similar cases it would be difficult to advocate radium in preference, because experience shows that adenocarcinomas vary considerably in radioresistance

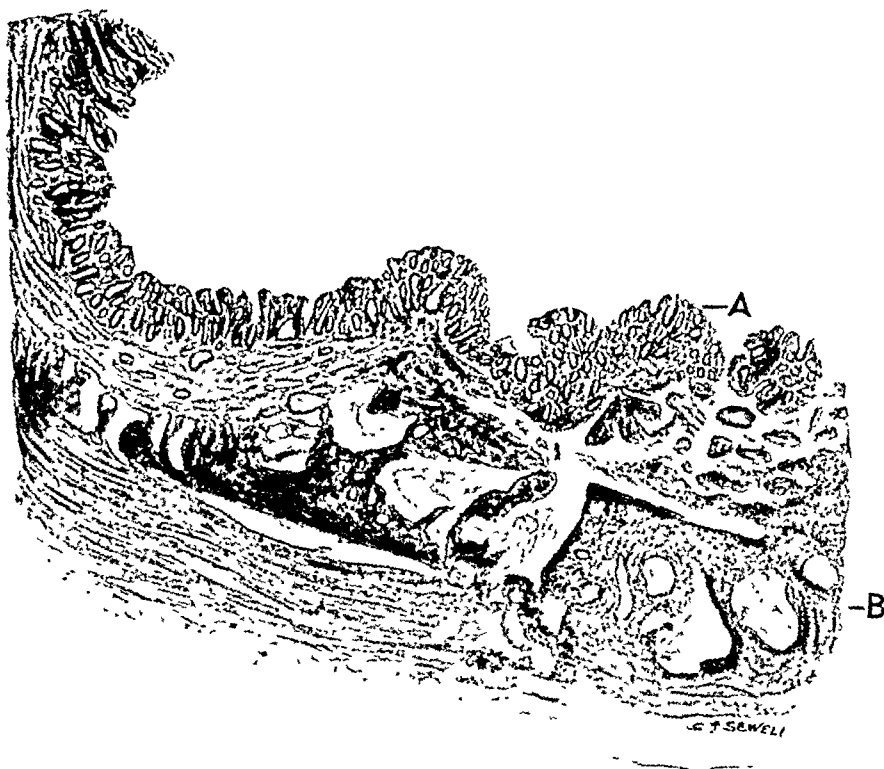


FIG. 2.—The section shows several collections of malignant cells in the submucosa and muscles, but the surface of the ulcer is covered with a thin layer of granulation tissue incorporating some healthy glands. The appearances are unknown in untreated cases, and indicate an attempt at healing and regeneration of the surface epithelium. A.—Regenerated epithelium. B.—Areas of mucoid degeneration.

and in their response to radiation, and so, unfortunately, the result which may be anticipated with radium in any given case cannot be predicted.

All growths of the rectum are regarded as operable, in the absence of metastasis in the peritonæum or liver, provided that the rectum can be removed with the surrounding tissues and all invaded lymphatics clear of the growth, and provided that the rectum is not fixed to bladder, sacrum, or pelvic wall by malignant infiltration. So that an A, or B, and many of the C cases belong to this class. As the growth extends from an early C to a late C so the suitability for radical operation diminishes. Somewhere between these two is the borderline case which is submitted or not to radical operation according to the age and general condition of the patient.

Though in most instances a good case cannot be made out for radium in

the early case in preference to modified radical surgery, there is much more to be said for it as the case approaches the borderline where a radical cure from radical surgery becomes more uncertain and the operative risks increase.

It is not possible to make any statistical comparison as to results in this class but when in doubt as to the wisdom of attempting a radical cure with surgery the surgeon is fully justified in employing radium, provided that he adequately radiates the entire growth and the lines of lymphatic spread in a uniform manner.

The ultimate result, as regards function of the rectum after radiation of

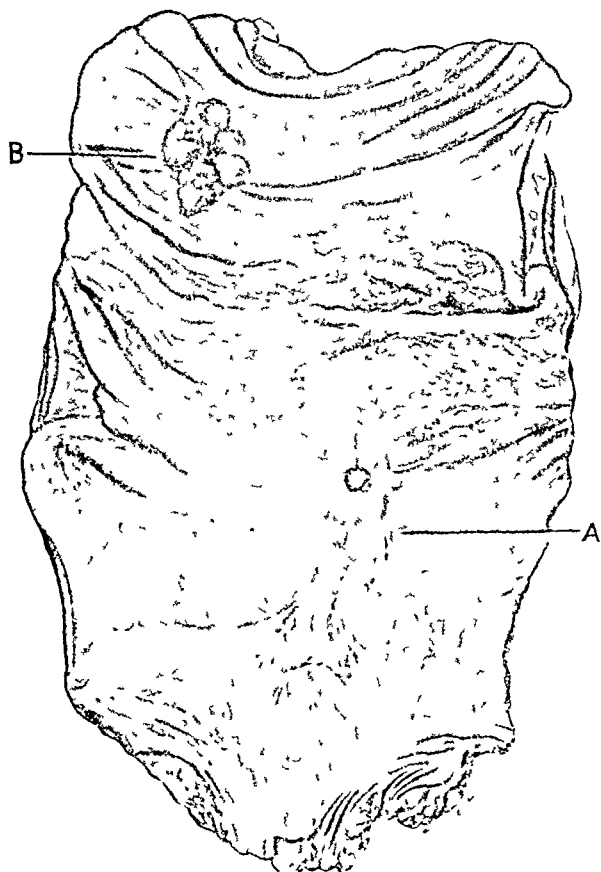


FIG 3—Results of radiation Rectum excised for carcinoma shown at B At B there is a puckered scar resulting from radiation of a carcinoma nearly three months before the second growth was discovered No carcinoma could be discovered on section of tissues behind the scar The small nodule at the upper end of the scar was quite soft The growth treated was about  $1\frac{1}{2}$  inches in diameter (Mr Gabriel's case)

a growth, varies according to the degree of fibrosis which results and whether or not a fibrous stricture follows. The smaller the growth dealt with, the better the prognosis as regards stenosis. Small growths can be destroyed with little or no deformity of the lumen. The degree of fibrosis depends also on variations in reaction. An overdose may cause necrosis and excessive fibrosis with resultant stricture, but a correct dose may secure a perfect result. New epithelium grows over the radiated area (Fig. 408) and it may be difficult to recognize any abnormality of the lumen on digital examination beyond a slight projecting ridge (*Vide* Fig. 3).

Alteration in the size of the lumen of the rectum results from local resections and fibrous strictures are very liable to follow, unless great care is exercised in avoiding sepsis during healing, and unless any tendency to stricture is checked by careful dilatation during convalescence.

When the operative risks of radical excision as distinct from local resection are considered, especially in cases where the risks are above the average, the arguments in favor of radium are more worthy of consideration.

If, in the future, adenocarcinoma can be graded like squamous-celled carcinoma of the tongue into radiosensitive and radioresistant, the arguments in favor of radium in selected cases may be enhanced. Hitherto, attempts,

prior to treatment, after removal of a small portion of growth, to differentiate and classify a case histologically have not been fruitful.

Furthermore, if research should reveal some method of sensitization which can be relied on, there will be a wider field for the use of radium in preference to surgery.

At the present time the number of cases dealt with in this class does not justify a too dogmatic opinion. The result in any given case depends on the delivery of an optimum dose, which is dependent on the correct amount of radium, the correct distribution, the correct filtration, and correct time of exposure.

Several unexpected failures have been encountered in the radiation of early growths. Fortunately, in most instances, these failures can and have been made good by radical surgery, but unless it can be shown that pre-operative radiation increases immunity against recurrence patients so treated may have cause for complaint.

Until a much larger series of early cases comes under review it is reasonable to assume that unexpected failures (such as two apparently similar growths treated on supposed identical lines, responding in one case well, in the other badly) may be explained in part by some error in technic and not entirely by variation in radioresistance.

*The Treatment of an Operable Growth with Radium.*—A small operable growth in the rectum below the peritoneal reflection and clear of the anal canal can, if it involves the anterior or lateral wall in the female, be attacked with needles through the vagina without surgical exposure. In the male the best approach is from behind after removal of the coccyx when the rectum can be mobilized so that the growth becomes accessible whether posterior, lateral or anterior. The same approach is employed for the female if the growth is posterior. If the growth, though small, has commenced to ulcerate, there is a risk of lymphatic spread, and whether the posterior or vaginal route is employed the retrorectal space should be radiated.

If a very small growth (not larger than a penny) is encountered and found to be malignant, and the mobility of the growth is such that it can be freely mobilized from the muscular wall (*i.e.*, an A case) it may be treated with some confidence by the introduction of intrarectal filtered radon seeds without surgical exposure and without glandular attack, though the fact that must not be lost sight of that local resection without colostomy offers in all probability a more certain cure, if the results of Doctor Dukes' investigations are not subject to error.

During the past five years, the author has dealt with over a hundred cases of cancer of the rectum with radium, and lest it should be supposed that radium has been preferred to surgery when surgery is indicated it may be mentioned that over sixty cases have been submitted to radical surgery during the same period.

For every case that has been submitted to radical surgery (or radium treatment), more than one has been found on exploration to be suffering

from secondary visceral deposit and submitted to colostomy only. Of the cases treated with radium only twenty-seven have been regarded as suitable for radical surgery. Some of these have refused colostomy or radical surgery; others have been given the choice. Five of these cases so treated have been subsequently dealt with by radical surgery because the radiation has been either incomplete or inefficient, or has been followed by recurrence, and are now well. Six are apparent cures for varying periods from one year to two and one-half years. One died after excision of the rectum following recurrence. One died after excision of the rectum following preliminary abdominal radiation. One remained well for a year and nine months and died following closure of colostomy. The remaining thirteen (including five cases of carcinoma of the anus) are under observation after treatment for less than a year; one of these has received secondary radium treatment, and another is under treatment with deep X-ray therapy following rapid recurrence. Space does not allow a discussion on technic and dosage but it is important to note that one of the disadvantages of radium treatment consists in the length of time (often two months) which these growths take to completely retrogress and disappear in most instances.

While evidence of growth remains there is uncertainty as to the end-result. When all visible growth has gone a varying amount of fibrosis remains. Uncertainty as to whether any growth remains in the interstices of these fibrous nodules cannot be avoided.

Further, when operative exposure from behind has been the method employed, the wound usually takes as long to heal or longer than after a radical excision. A long operative convalescence can be endured patiently if the prospect of cure is assured, but not so if the prospect remains throughout an uncertain one.

For the very early accessible growth there is much to be said for vaginal or intrarectal (or perirectal) radiation without surgical exposure. If this fails, surgery can follow without delay. Healing is not inhibited after radiation provided that the interval between radiation and operation is not long enough to allow marked fibrosis and diminution of blood supply.

It will be noted from this brief summary that it is too early to report definitely on the results of radium treatment for the operable case.

Nevertheless results show that even when a growth has not penetrated through the bowel wall and is small enough to be accessible to uniform interstitial radiation by one method or another, radium may fail, possibly not always due to want of sensitivity to radium but to imperfect technic. Some of these radium failures have been relieved by radical surgery after a prolonged period of treatment. Even in those cases which remain well without colostomies and with apparently healthy rectums the question of future recurrence is still *sub judice* and on a less secure foundation probably than after resection.

The cases which have so far been considered are those cases of early carcinoma which are situated below the peritoneal reflection and are easily

accessible to interstitial radiation on the one hand or to local excision on the other.

Two other classes of operable growths remain for consideration:

(1) Those which are above the peritoneal reflection and must, if treated surgically, be submitted either to perineal or abdominoperineal excision with colostomy, or if treated with radium cannot be satisfactorily dealt with except by transperitoneal attack.

(2) Operable cases of squamous-celled carcinoma of the anus.

(1) During the past three years the author has employed radium (both needles and seeds) by the transperitoneal route. (*Vide* Fig. 4, *British Journal of Surgery*.)

(a) To barrage the upward line of lymphatic spread along the inferior mesenteric vessels as a preliminary to radical excision (at the time of colostomy).

(b) To attack the fixed, inoperable growth which is situated above the peritoneal reflection, or to deal with the upper part of a growth which lies partly above and partly below the peritonæum.

(c) To attack an operable growth above the peritonæum in a patient who is considered too old or too unfit to stand an abdominoperineal excision.

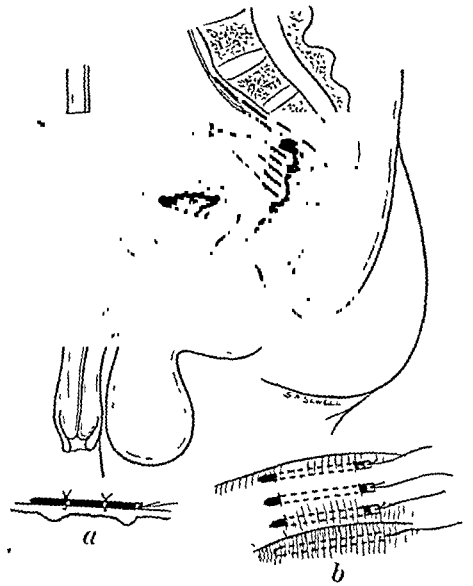


FIG. 4.—Abdominal radiation with needles; a and b, alternative methods of using needles within the abdomen.

Transperitoneal radiation is a far more risky proceeding than perineal radiation. Radium causes a variable amount of inflammation of the peritonæum, often with effusion of fluid in the area attacked, and if this area is not protected from the small gut and drained, there is a risk of paralytic ileus. Further, if the lumen of the bowel is penetrated by a needle and a track is established between the lumen and the peritoneal cavity as the result of radium necrosis, there is considerable risk of general peritonitis.

Experience has shown that the use of radon seeds within the abdomen causes far less disturbance to the peritonæum than radium needles, and is a much safer proceeding, but so far the end-results have not been so encouraging. In the author's experience this observation applies to most other regions treated with radon.

The radon seeds can be left *in situ* and have not so far caused any harm. The removal of the needles often calls for a second anæsthetic.

In only eight cases has radium been employed within the abdomen for a growth above the peritoneal reflection which might have been excised.\* In

\* Three of these were labeled as "borderline" and have not been included in the twenty-seven operable cases treated with radium. For the purposes of this paper the total should read as thirty.

one of these, seeds were inserted when there were no facilities for radical operation. Subsequently, in another place, excision of the rectum was performed, and the patient died from recurrent hæmorrhage (case already referred to). A microscopic section of the growth after removal is shown (Fig. 2†) and it is most instructive to note that five weeks after radiation new epithelium has commenced to grow over a granulating area and that most of the underlying growth has undergone *mucoïd degeneration* with here and there a few islands of carcinomatous cells. It seems possible that, if operation had been delayed, the growth might have been destroyed with radon and the operation not required.

The other seven cases have all done well but it is not possible to say that any one of them is cured. In each instance, if operation had been carried out, an abdomino perineal excision would have been necessary and was decided against on general grounds.

A number of cases have been treated by transperitoneal radiation under heading (b), which does not come under discussion in this paper, but it may be mentioned that one of these is an apparent cure (two and one-half years) and has no colostomy.

(2) Squamous-celled carcinoma of the anus stands on a somewhat different footing from adenocarcinoma of the rectum.

Early cases, which have not infiltrated deeply into the ischio-rectal fossa, surrounded the anus or invaded the inguinal glands can, I think, be promised an immediate cure with interstitial radiation, combined in some instances with surface radiation. The question of permanent cure cannot yet be answered. So far results in these cases have been excellent with one exception, the case already referred to, in which recurrence followed an apparent cure. This was the first case of the kind treated (1925). Recurrence occurred wide of the original growth and it is probable that the periphery of the growth was inadequately radiated.

There are distinct advantages in the use of radium in these cases over surgical excision.

Radical removal of an anal growth involves removal of the sphincters and a colostomy, whereas with radium in most early cases complete restoration of rectal function can be secured and a colostomy avoided.

### CONCLUSION

It is common knowledge that in young people (under thirty years of age) carcinoma of the rectum grows rapidly, gives rise to early metastasis, and usually recurs after radical excision. I have notes of eleven patients under thirty years of age whose rectums I have excised. Not one of these survived three years.

So far as inoperable growths are concerned, the best results which have been secured with radium have been in patients under forty. The same holds good though not to so marked an extent with the operable case.

I have not much evidence to support my view, but I am inclined to think

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† Fig. 408 in *British Journal of Surgery*, Vol. xvii, 1930.

that though there is little hope for a patient under thirty afflicted with carcinoma of the rectum, however treated, he has more chance of a cure with radium than with surgery. The more active the growth the more radio-sensitive it is.

When dealing with cases of adenocarcinoma of the rectum below the peritonæum, except in the very young, it is impossible not to conclude that with the experience available at present the results which may be anticipated are too uncertain to justify preference for radium to surgery unless surgery is refused or contraindicated on some general grounds or the growth is on the borderline between operable and inoperable.

The operative risks of dealing with high growths of the rectum by the abdominoperineal route are considerable so that unless the case is considered to be an exceptionally good operative risk and the growth is sufficiently early to give promise of freedom from recurrence, the employment of radium can be justified. In such cases colostomy may sometimes be avoided with radium treatment, but never with operative treatment.

In cases of squamous-celled carcinoma in the early stage there are strong arguments in favor of the use of radium in preference to surgery. If this fails, colostomy and excision still may be employed in the majority of cases as a radical measure.

It need hardly be added that increased knowledge of the action of radium and greater experience in technic may improve results vastly and modify our views as to its utility in relation to surgery.

At the present time incomplete knowledge and limited experience of the action and use of radium have to be balanced against a standard of surgery which seems to have reached its zenith.

At present radium is like a wild horse which must first be tamed, before it can be harnessed to the surgeon's team. Whether it will take a place as leader, or wheeler, or as a spare, remains to be seen.



# FAR-REACHING EFFECTS OF GAMMA RAYS AND SHORT X-RAYS UPON THE HUMAN HEART

ELECTROCARDIOGRAPHIC RESULTS OF CANCER TREATMENTS  
GIVEN WITHOUT DIRECT IRRADIATION OF THE HEART

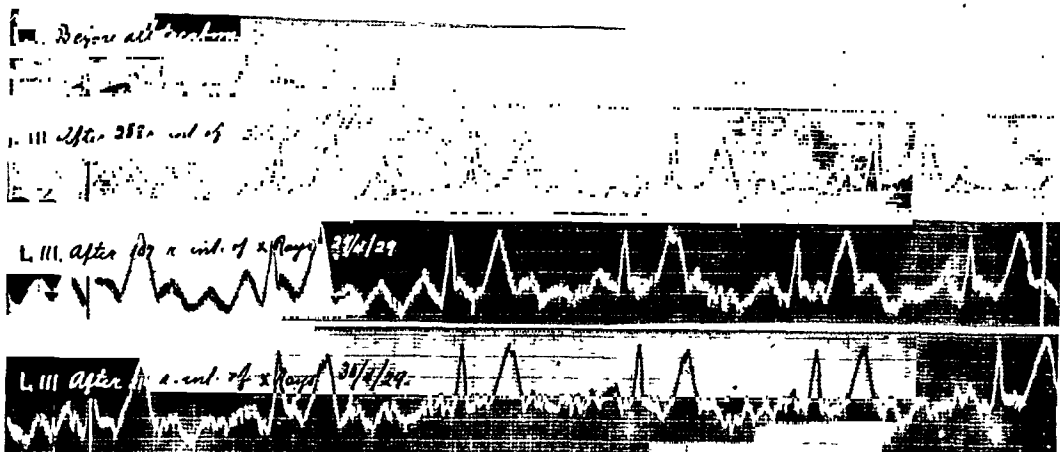
By J. E. GENDREAU, M.D.

OF MONTREAL, CANADA

FROM THE RADIUM INSTITUTE OF MONTREAL

CARDIOVASCULAR disturbances produced by large doses of gamma rays and short X-rays, even when the heart itself has not been directly treated, are accompanied by symptoms which are well known clinically: dyspnoea, tachycardia, general fall of blood-pressure, and asystolia in very serious cases (Coutard et Lavedan; Lavedan et Monod).

As electrocardiograms are helpful in the appreciation of these symptoms, and in the direction of the treatments, we have added systematically the electrocardiographic studies to our clinical examinations, before, during and after the treatments by radium and X-rays.



CASE Ia.—Male, seventy years. Sarcoma of the left leg. Treated by large doses of X-rays—5350 international r. distributed over four fields, in four series of treatments, during twenty-five hours of actual irradiation.

*First Series.*—Intensive treatment, twenty-eight sittings of thirty minutes each—2996 int. r. in seven days. The records show a marked reaction upon the heart: slower rhythm, higher *Q R S* voltage, high amplitude and long duration of *T*—auricular flutter—diphase and multiplied *P* waves. The tracing presenting such irregularities, a complete rest is ordered for fifteen days.

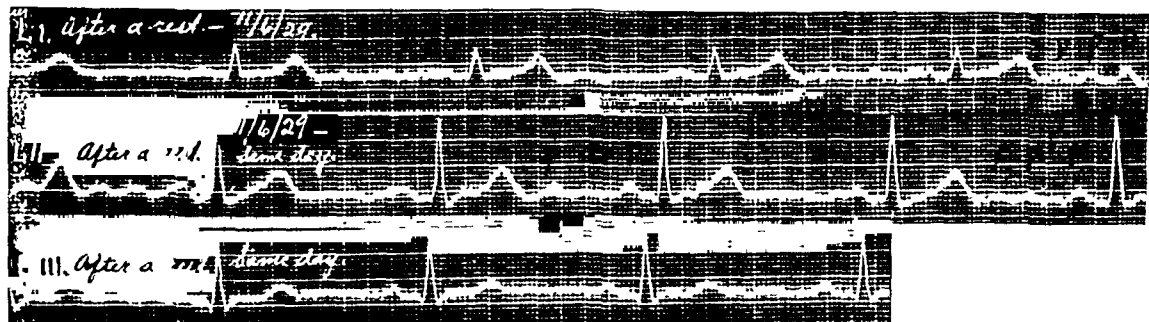


CASE Ib.—*Second Series.*—The records of the three leads *before* treatment are more normal. The rhythm is still slower than before the treatments, but the voltage is higher, *S* deeper. After the treatment of two hours of X-rays, three sittings, 407 int. r., the same effect is obtained as in the first series, but with less intensity.

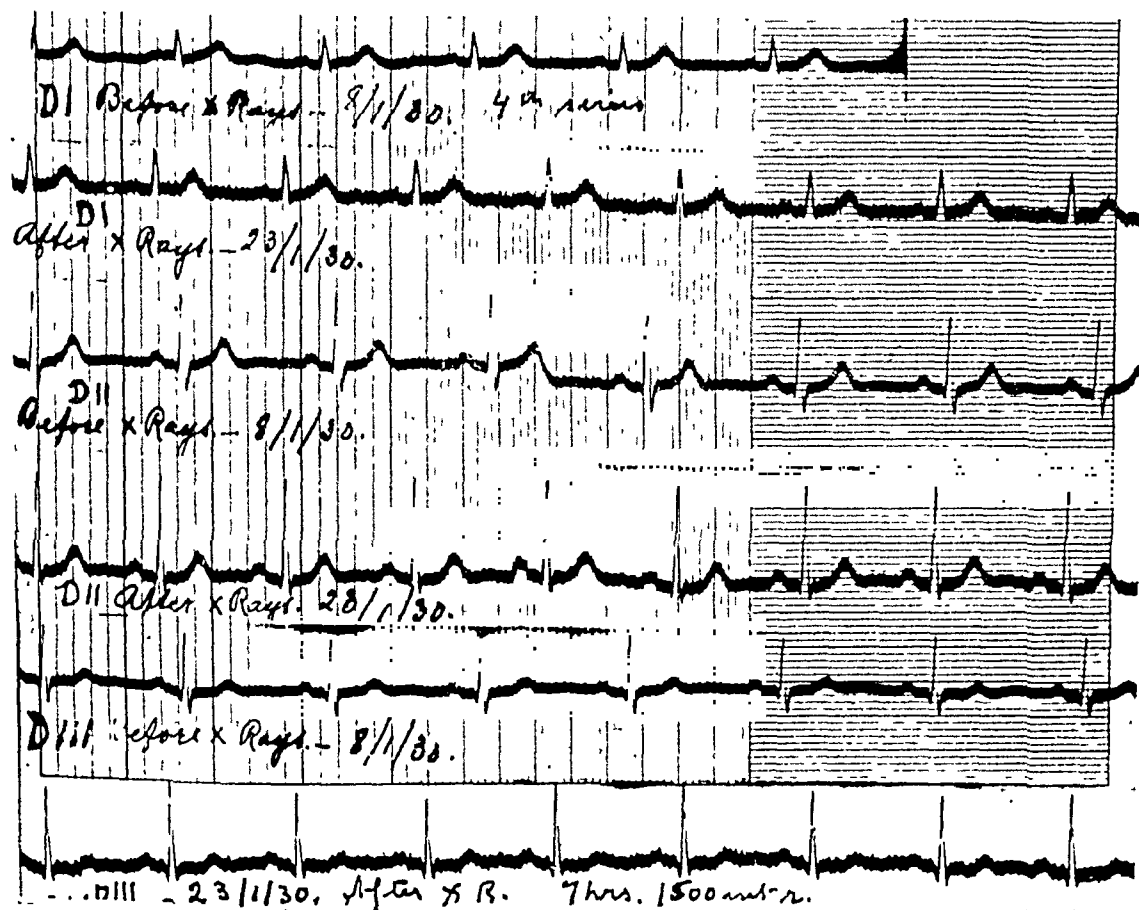
## EFFECTS OF RÖNTGEN-RAYS ON HEART

We have many records taken in cancer cases when the irradiation area was outside the region of the heart, which, moreover, was sufficiently protected against external secondary radiation.

Different types of cancers were chosen, of different malignity, localized, or with metastases, at their onset or well advanced, in different patients, male and female, from ten years of age to seventy-three, in good or bad general condition. Cancers of variable parts of the body—lip, tongue, cheek, neck, right arm and axilla, right breast, bowels, uterus and leg. Cancers treated by radium alone, or X-rays alone, and by radium and X-rays combined, in massive, or in long-protracted doses.

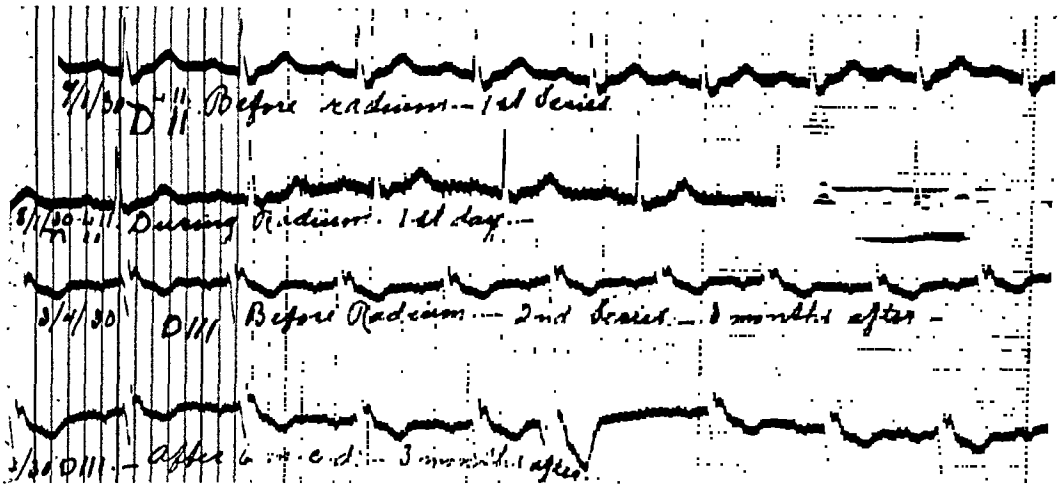


CASE Ic.—A record of the three leads taken a month after the second series: the heart is still fluttering, the T waves are high, and the voltage lower in lead I.



CASE Id.—Fourth Series.—Six months after. Before treatment the heart is in a fair condition. 1500 int. r. are given in fourteen sittings of thirty minutes each distributed over fifteen days. The reaction is evident but mild; the voltage is increased in the three leads, the rhythm is quicker, and the tracings show fine undulations after treatment. It follows that the reaction upon the heart can be mitigated by cautious treatment when the intensive dosage is not imposed by the evolution and nature of the tumor.

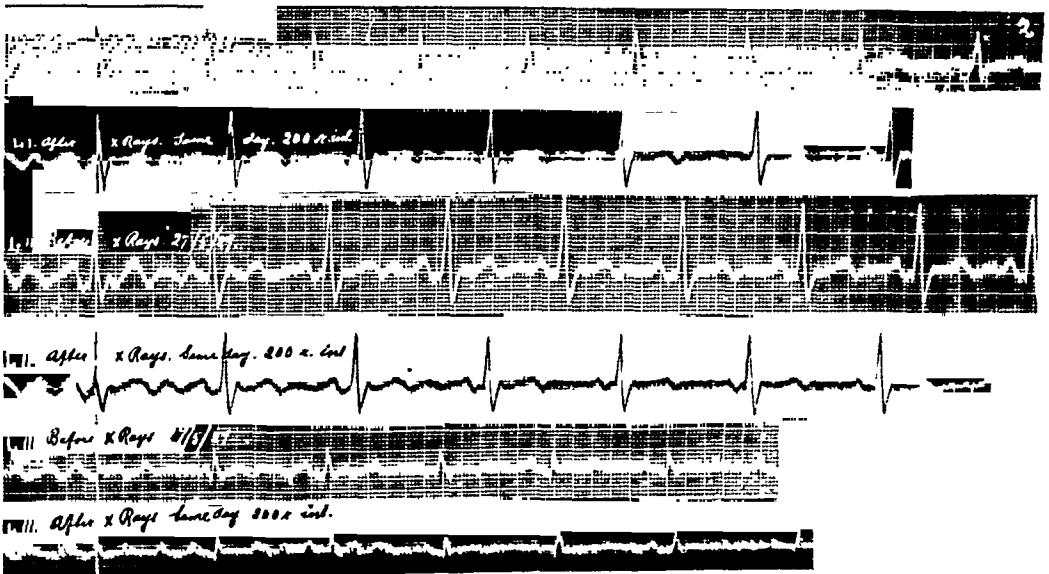
*Technic.*—(1) *Gamma Rays or Curietherapy.*—The methods of l'Institut du Radium de Paris were generally applied. Radium sulphate and radon were used in surface applications, and interstitially in needles. Filtration: 0.5 millimetre to 1.5 millimetres of platinum, or 2 millimetres of lead in surface applications, with aluminum, felt and Columbia paste. Distances to the skin: from 1 to 6 centimetres. Moderate prolonged doses. Measuring instruments: electroscopes and Mallet's ionomicrometer with water phantoms.



CASE IIa.—Woman, sixty-three years. Cancer of the left cheek recurring, treated with radium, 11 m.c.d. in fifty-nine hours, in two series of applications.

*Leads II.*—Before and during radium, on the first day of the first series. The record after treatment shows a slower and irregular rhythm, fine auricular fibrillations with flattening of the P waves, notchings of the ascending branch of T.

*Leads III.*—In the second series, three months later, show after radium a slower and irregular rhythm, a premature ventricular contraction, with deformity of the Q R S complex—the decrease of Q persisting after the compensatory pause. Deeper inverted T. Serrated inverted P waves.

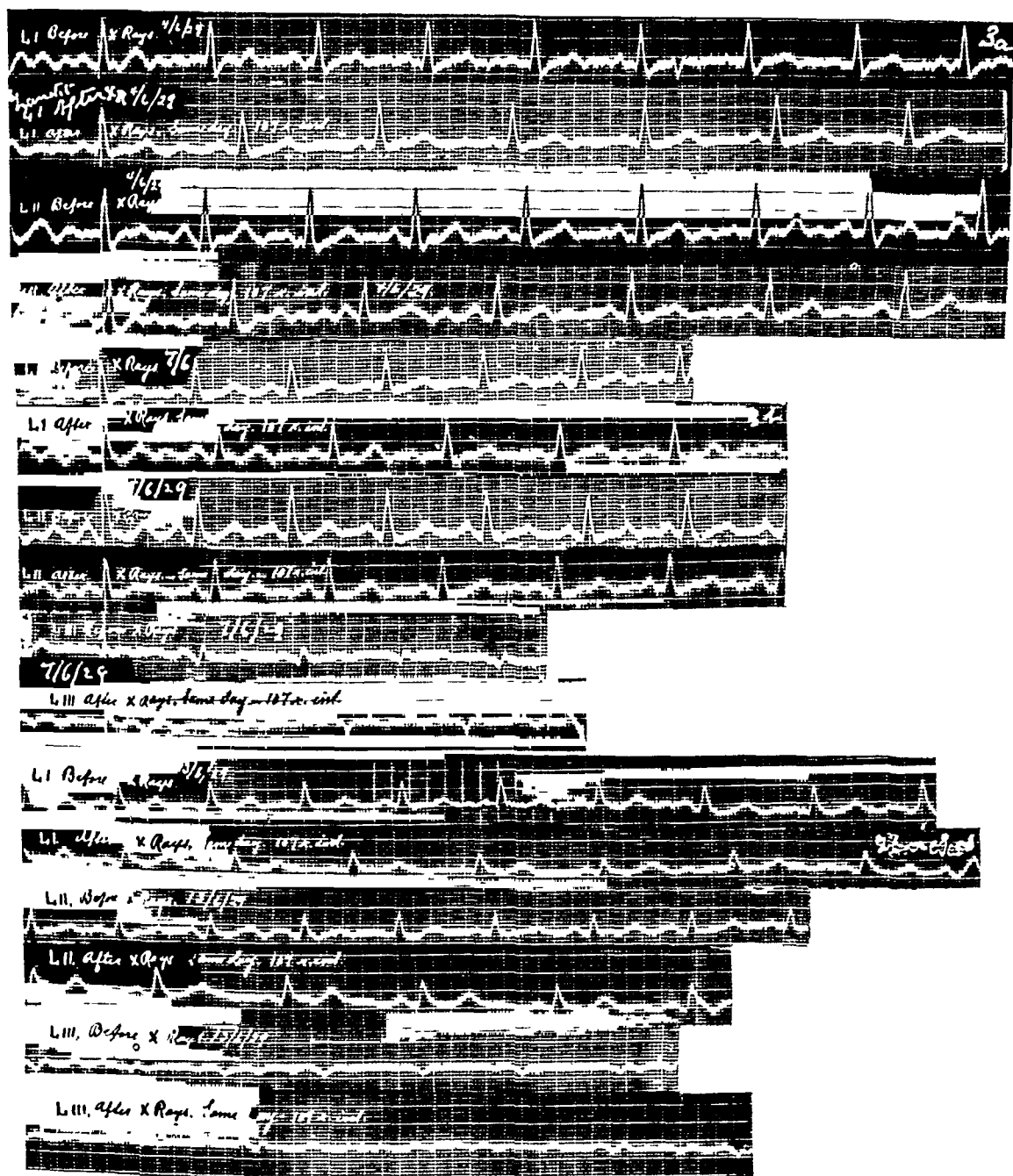


CASE IIb.—X-ray Treatment.—The records before treatment in the three leads, showing a better state of the heart, heavier X-ray doses are given, 200 int. r., in one sitting. The effect is immediate upon the tracings in the three leads taken just after treatment: slower rhythm, lower voltage, in II and III, deeper S in I and II, flattening of the tracings, more flutter and fibrillations in all the leads.

(2) *X-ray or Röntgen Therapy.*—Apparatus: mechanical rectifiers (Standard, Kellykoet); constant potential generators (Gaiffe-Galot-Pilon). Voltages: from 165 kilovolts to 185 kilovolts measured by sphere gaps, calibrated voltmeters (Abraham-Villard-Carpentier), spectograph. Standard Coolidge tubes (G. E. and Gaiffe-Galot-

## EFFECTS OF RÖNTGEN-RAYS ON HEART

Pilon) in the air; the patient being protected by lead cylinder (Wappler), or box (Standard), special large enclosing lead-glass receptacles, (two models from l'Institut du Radium de Paris), all motor ventilated; additional thick lead-rubber sheets. Intensity from 2.5 milliamperes to 3.5 milliamperes. Focal skin distance 50 centimetres. Fields at the skin, from 130 square centimetres to 230 square centimetres. Filters: zinc



CASE IIC.—Eight double tracings *before* and immediately *after* X-ray sittings on three different days, showing the same comparative changes in all the leads: slower rhythm after treatment, decrease of the voltage, especially in lead III, additional *P* waves.

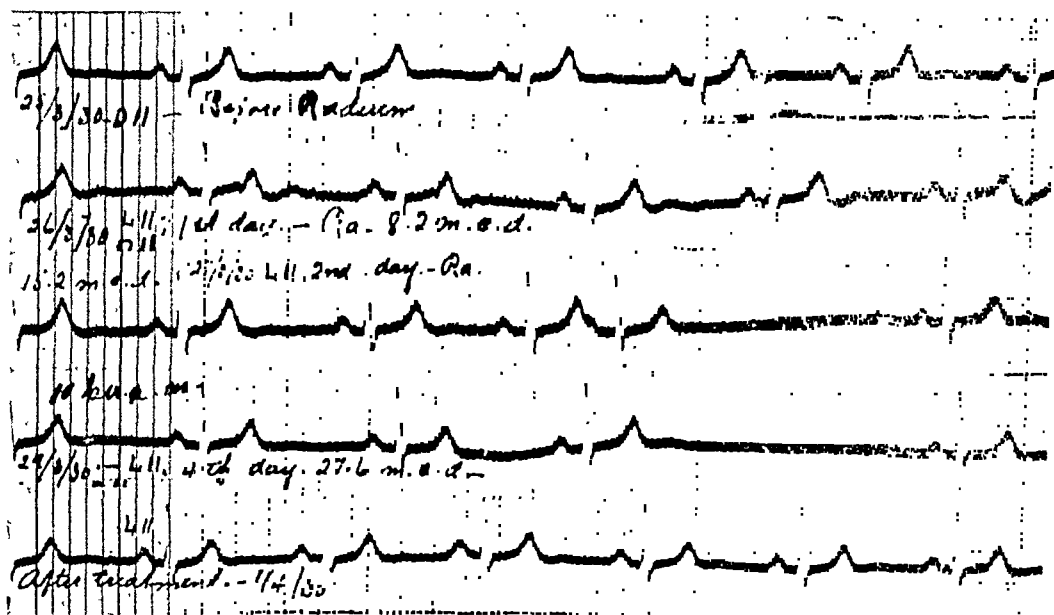
2 millimetres or copper 2 millimetres plus 1 to 3 millimetres aluminum. Percentage of transmission from 42 per cent. to 50 per cent. through 10 centimetres in water phantom (Solomon Beclere). The doses were measured with ionometers (Solomon-Fricke-Glasser) calibrated, and checked with radium, and with the large Kustner's air ionization chamber, from Germany. The small chambers resting on the patients.

These are practical measurements made with ordinary care, but not with the physical laboratory accuracy.

(3) *Electrocardiograms*.—Taken with Boulitte or Victor's G. E. apparatus, with apparently independent electrical sources; but in the tracings the fine heart undulations are often combined with parasitic 60 cycle waves, causing too-frequent notchings.

Dr. L. Jutras assisted in taking out the electrocardiographs.

In each case the changes are appreciated by comparison with the tracings taken *before* treatments. The records show the action of the gamma rays and X-rays upon the heart at a distance; by additional *P* waves, and impure flutter; by flattening of the *P* waves, and auricular fibrillation; by abnormal *Q R S* complexes, in general with lower voltages and reduction of the tracings to a line, occasionally with maximum voltages—very deep *Q* and *S* deflections; by deep inverted *T* waves, sharp and rounded, with occasional notchings in the ascending branch. *R T* is constant but *T P* is generally increased and



CASE IIIa.—Male, fifty-three years. Extensive cancer of the lower lip with gland metastases. 50 m.c.d. of radium in six days.

Leads II.—Five tracings, one before, three during radium, one after. The records during treatment show:

On the first day, slower rhythm, fine undulations, additional *P*, notchings in the ascending branch of *T*—depressions after *T*. On the second day, premature ventricular contractions, *T* being immediately followed by *P*, compensatory pause. On the fourth day, persistence of the arrhythmia—with pauses.

Leads II become quickly normal after the cessation of the treatment.

the resulting rhythm slower immediately after a treatment. In premature ventricular contractions on the contrary, *T P* is greatly reduced and *P* immediately follows *T*. The extra systole is generally succeeded by the compensatory pause. Tachycardia is less common than bradycardia.

There is no available space in the article for discussions about the influencing factors of fields, volumes, intensities, time, general condition of the patient, location of cancer, age, difference in after-effects of radium and X-rays, duration of the effects. It is, however, evident that electrocardiograms may be useful in the direction of a cancer treatment by irradiations.

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## CONCEALED CANCER OF THE TONGUE\*

BY WILLIAM F. MACFEE, M.D.

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IN SPITE of the fact that the tongue is an accessible organ, there is a discouraging number of failures to recognize early lingual cancer. Delinquency on the part of the patient is sometimes responsible, but with increasing public education on the subject of cancer the patient is becoming less frequently to blame. An impressive number of failures must be attributed to the medical profession.

Diagnostic failures come about in two ways. First, the lesion is discovered but not recognized as being cancer. It is mistaken for some benign condition, such as an aphthous ulcer, syphilis, or a traumatic lesion. This is a large and interesting group but must be omitted from the present discussion. We are now concerned with another group in which the lesion is not discovered. It is not discovered because it is partly concealed and because the symptoms are not recognized as pointing to the tongue. Of seventy cases reviewed in the preparation of this paper a little more than 20 per cent. belonged to this group.

There are two clinical types of cancer of the tongue which may be called concealed. There is the type which conforms to the classical descriptions of cancer but which escapes detection because of its situation. Cancers of this kind are located far back on the tongue, usually in its pharyngeal portion. Favorite sites are those at which there is angulation of the lingual mucous membrane as it merges into the mucosa of adjacent structures, as at the base of the pharyngeal tonsil or of the tonsillar sinus, at the lingual attachment of the glosso-palatine arch, in the valleculæ, or at the glosso-epiglottic fold. The other clinical type of concealed cancer escapes detection because it is almost completely buried in the substance of the tongue. This type is nearly always in the posterior half or two-thirds of the tongue and is found most often on the inferior surface of the oral portion of the tongue where its mucous membrane reflects onto the floor of the mouth. Fitzwilliams<sup>1</sup> describes varieties of it as the indurated plaque and the nodulated induration. It differs most strikingly from the usual conception of lingual cancer. Cancer of the tongue is most often described as a foul, irregular ulcer, with uneven and sloughy floor and with rolled-out, hardened edges. On the contrary, the external ulcer of the infiltrating type of concealed cancer may be very small, or indeed missing, whereas the tumor mass may be large and deeply invading. There is usually a slight dimple, or pucker in the mucous membrane over the most superficial part of the tumor.

\* Read before the New York Surgical Society, October 8, 1930.

Here there may be a slight loss of epithelium or it may be intact. Often there is a slight pallor of the surrounding mucous membrane. Just why there should be such deep invasion with so little external ulceration is not apparent. Histologically, the tumor is squamous-celled and not of adenomatous origin. This form of cancer may involve a large part of the tongue before it is discovered by either the patient or his physician.

The two types of hidden cancer just described are not usually detected in the course of a routine clinical history and examination. The symptoms of early cancer of the tongue are not those of advanced cancer. It is unfortunate that pain in the tongue is still listed as an important symptom of cancer. Pain is very likely not to be an early symptom. This is particularly



FIG 1.—Showing depression over the centre of the lesion under the tongue; mucous membrane is intact

true if the lesion is located in the less sensitive posterior portion of the tongue. In general, it may be said that there is a striking absence of early symptoms which point directly to the tongue. Such symptoms as are present may be more or less indirect and therefore misleading. A routine examination of the tongue may also be fruitless. A cancer situated far back on the tongue, even if ulcerated, is not seen unless the laryngeal mirror is used. A cancer lying almost wholly within the substance of the tongue likewise escapes observation, even when the tongue is thrust far out. Having the patient elevate the tongue may reveal suggestive signs if the growth is well forward. When, however, it is in the posterior half or two-thirds, raising the tongue merely serves to further obscure the growth, because when actively elevated the

tongue is automatically retracted at the same time.

The palpating finger is much more reliable than the eye in detecting cancer of the tongue. If the tongue is relaxed during the examination, an indurated area, unless it is very far back, will nearly always be felt. If, however, the tongue is thrust out, its muscles are hard and a zone of induration may be missed. Valuable as the procedure is in the discovery of cancer, palpation of the tongue is not ordinarily done by the examining physician, unless something is suspected. The patient likewise rarely touches his tongue with the finger unless he senses some change in it, and it is surprising how large a growth in the posterior part of the tongue may become without giving appreciable local symptoms. The following case histories are illuminating:

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CASE I.—Hosp. No. 79423. White, female, thirty-seven years old. About August 1, 1929, the patient began to notice that when drawing her tongue in she had "an unnatural sensation" in the posterior part of it. Soon afterward, perhaps a few weeks, she developed several "canker sores" on the left side of her tongue and on the inside of her left cheek. She consulted a surgeon who made a microscopic examination and found that she had Vincent's angina. The lesions were treated locally with an arsenical solution applied with cotton for an hour or so at a time. Treatment in this manner was continued for three or four months. All of the sores healed and the patient felt well except that she had considerable pain in the back of the tongue when she yawned.

About a month later she developed a blister-like pus pocket in the region of the left tonsil. She was seen by a second surgeon who incised it. There was a good deal of bleeding but the patient did not see any pus. The wound seemed to heal, but about two weeks afterward the patient began to have a sticking pain in the left ear, pain in the left side of the head, and along the left lower jaw. Soon a swelling appeared in the left posterior portion of the tongue very near the tonsil. White patches developed about this area, on the tonsil, tongue, and soft palate. The tongue became hard and "knotted up" so she could not use it. Further examinations by a number of surgeons confirmed the original diagnosis of Vincent's angina. Intravenous treatment was carried out but no improvement resulted. After one month the swollen area was incised. This was followed by further intravenous treatments and local applications. The condition became rapidly worse. The patient was sent to a sixth surgeon whose description of the lesion follows:

"There is a triangular ulcer on the under surface of the left border of the tongue opposite the first and second molar teeth. This is an inverted triangle in shape, 1 by .5 centimetres in diameter. It has a clean, red surface and a low border. From this start there has been an invasion into the tongue substance posteriorly through the entire left half of the tongue as far as the epiglottis. In this latter region the infiltration has broken through the surface to form a typical cancerous ulcer 1.5 centimetres in diameter. The left soft palate shows invasion which is continuous with an induration about the left tonsil, but the recent incision at the tonsil may have been followed by an inflammatory reaction to which the tonsillar induration could be ascribed. The infiltration of the tongue definitely limits the degree of motion. Apparently there has been an extension beyond the region of the tongue itself except that in the soft palate. The submaxillary and deep jugular chains of lymph-nodes are involved. The condition is wholly inoperable."

The diagnosis of cancer was confirmed by biopsy and palliative radiation instituted. The patient died two months after the diagnosis was made and ten months after the onset of symptoms. In this case Vincent's angina may have preceded or have been subsequent to the onset of carcinoma. It is evident that attention was so completely centered on the infectious process that the cancer was overlooked.

CASE II.—Hosp. No. 70050. White, male, fifty-one years old. For about six weeks the patient has suffered from almost constant pain in the upper abdomen. The pain is severe and radiates across both sides of the abdomen, to the lower anterior chest, and to the back in the region of the shoulders. The pain is not definitely related to meals but usually comes on within a few minutes after he has eaten and lasts for two or three hours. The patient has often felt as if something prevented food from passing through his stomach. He also has some discomfort in the throat when swallowing, and now takes nothing but soft food and liquids.

In addition to this stomach trouble the patient has had persistent neuralgia in the left side of the face and jaw, the left side of the head, and in the left ear. He sometimes feels as if someone were jabbing an icepick in his ear.

*Past history.*—No history of venereal disease; is a heavy smoker of pipe and cigars; alcoholic stimulants in moderation.

*Family history.*—No malignant disease.

*Examination.*—The mucous membranes of the mouth are of good color. Teeth



sound, except for some peri-dental gingival infection. Tonsils small, pharynx slightly injected. The protruded tongue deviates slightly to the left. No palpable lymph-nodes in the neck. Heart and lungs negative. Abdomen negative. Genitalia negative. Patellar reflexes diminished.

*Laboratory findings.*—Urine negative. Blood Wassermann negative. *Radiographic findings.*—Barium meal. Pylorus and duodenum negative. Some constant irregularity of the cardiac portion of the stomach suggestive of a defect. No six-hour retention.

*Laryngeal examination.*—The laryngeal box is tremendously large but anatomically and physiologically normal. There is a swelling beneath the left side of the tongue about the level of the last molar. The tongue deviates to the left. Suggest X-ray with the possibility of finding a stone in the submaxillary gland.

*X-ray report.*—No evidence of stone in submaxillary gland.

*Neurological examination.*—Pupils small and slightly irregular, react to light and accommodation. The tongue deviates to the left because of fixation to the floor of the



FIG. 2.—Longitudinal section through the tongue of patient shown in Fig. 1. Note deep invasion toward center of tongue. An area of cystic degeneration is seen toward the tip.



FIG. 3.—Showing cancer invading tongue. Mucous membrane intact.

mouth. Left knee-jerk sluggish, right absent. Ankle jerks not obtained. No Romberg. The probability of an early tabes must be confirmed by spinal puncture.

On December 19, 1928, eight days after admission to the hospital, a more careful examination of the tongue revealed a hard tumor imbedded in the left half of it opposite the second molar. It seemed fixed in the substance of the tongue and was slightly sensitive to pressure. Inspection of the surface of the tongue revealed a little flattening on the dorsum overlying the tumor. The left inferior lateral surface of the tongue near the reflexion on the floor of the mouth showed an area .5 centimetres in diameter over which the mucous membrane was slightly retracted and fixed to the tumor. There was no ulceration, but the area had a slightly rough, or granular surface with a little grayish stipling. The patient was unaware of the presence of the tumor but after its discovery remembered that the tongue had recently "felt a little raw as if it had been scraped."

A diagnosis of cancer was made and on December 24, 1928, a hemiglossectomy was done. This was followed by excision of the lymph-nodes of the neck on both sides. No involvement was reported. The patient is well at the present time.

In this case the chief complaint was upper abdominal pain which radiated to the lower, anterior chest and to the posterior shoulder regions. This

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very misleading symptom disappeared immediately after removal of the lingual carcinoma and has not returned—now nearly two years after operation. We may conclude therefore that the pain in this case was not due to a peptic ulcer, for example, but to cancer of the tongue and that it was referred to areas of vagus distribution. It is noteworthy that this symptom is mentioned in only one other case of the group studied. We are reminded that the jugular ganglion of the vagus communicates with the petrous ganglion of the glosso-pharyngeal nerve by an inconstant branch (see diagram).

When cancer is located in the posterior half of the tongue one of the first and most consistent symptoms is pain in or about the ear and rarely in the tongue itself.<sup>1</sup> It is interesting that pain which presumably has its origin in the tongue is so constantly referred to the ear. In glosso-pharyngeal neuralgia, as described by Doyle,<sup>2</sup> Adson,<sup>3</sup> Dandy,<sup>4</sup> and others, pain in the ear is one of the most constant and most prominent symptoms. It would seem, therefore, that painful disturbances of the glosso-pharyngeal nerve tend to be referred to the ear. The tympanic branch of the glosso-pharyngeal is generally believed to be responsible.

Pain in the general region of the external ear may be explained in a similar manner. Harris<sup>5</sup> has pointed out that the sensory nerve supply in this region is very complex. No less than four cranial nerves take part in it. (See diagram) He gives them as: (1) The auriculo-temporal branch of the third division of the fifth nerve; (2) sensory branches from the geniculate ganglion of the facial, or seventh nerve; (3) Jacobson's nerve from the glosso-pharyngeal, or ninth pair; and (4) Arnold's nerve from the tenth or vagus. Since all of these cranial nerves inter-communicate, pain arising from the tongue and referred to the ear and thereabout may readily be accounted for.

The symptom next in importance to pain in the ear is a certain amount of what patients refer to as awkwardness of the tongue. By this is meant some disability in swallowing, in dislodging particles of food from the teeth, and occasionally there is some clumsiness of the tongue in speech. This probably is due in part to replacement of muscle by tumor tissue and sometimes to motor-nerve involvement.

A third symptom often mentioned or elicited is a queer, unnatural, or tickling sensation in the involved side of the tongue. This is likely due to sensory nerve disturbance.

These three symptoms, pain in and about the ear, motor disturbances, and painless sensory disturbances of the tongue, are to be emphasized as among the earliest and therefore the most important symptoms of cancer of the tongue. Salivation, pain in the tongue itself, fetor, and all of the text-book symptoms eventually appear, but by the time they are present the condition usually is hopeless.

The signs of concealed cancer of the tongue are often overlooked unless

cancer is suspected. Hints of its presence, however, may be derived from the following:

1. When the patient protrudes the tongue far out there is a tendency for it to deviate slightly toward the side of the lesion. (See photograph.) This is due in part to replacement of lingual muscle by tumor tissue and partly to terminal motor-nerve involvement which produces an incomplete paralysis of the affected side of the tongue.

2. Often a slight dimpling, furrowing, flattening, or other evidence of retraction of the surface mucous membrane may be seen.

3. Occasionally it is possible to detect a slight defect in the patient's speech. This results from mechanical disability of the tongue.

4. Inspection may reveal a minute ulcer at the most superficial point of

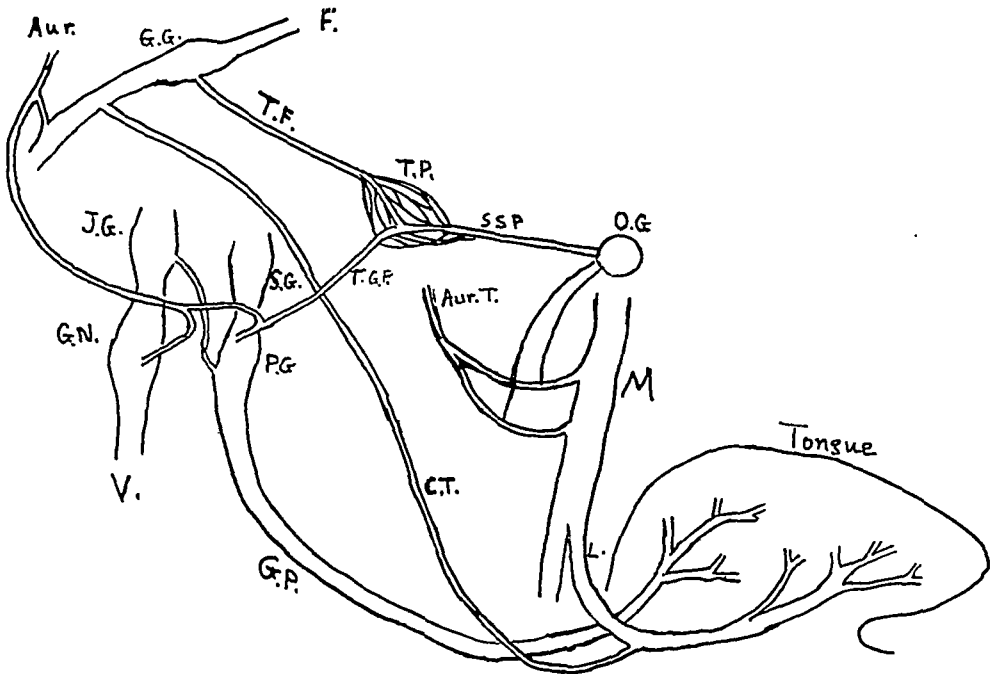


FIG. 4.—Schematic illustration of sensory nerve supply of tongue various communications. F.—Facial nerve. V.—Vagus. G.P.—Glosso-pharyngeal. M.—Mandibular division of the trigeminal. T.P.—Tympanic branch of facial. S.S.P.—Smaller superficial petrosal. T.G.P.—Tympanic branch of the glosso-pharyngeal. O.G.—Otic ganglion. Aur.—Auricular branch of vagus with communicating twig from sensory root of facial. Aur. T.—Auriculo-temporal branch of the mandibular. C.T.—Chorda tympani. J.G.—Jugular ganglion of the vagus. G.N.—Ganglion nodosum of vagus. S.G.—Superior ganglion of glosso-pharyngeal. P.G.—Petrous ganglion of glosso-pharyngeal.

an infiltrating cancer. Lesions of the pharyngeal portion of the tongue may be revealed by the laryngeal mirror.

5. Palpation properly done will nearly always reveal an area of induration.

6. Too frequently, enlarged, hard, lymph-nodes in the neck constitute the first observed sign of cancer of the tongue. Even then the primary lesion may be missed. We have records of such cases in which the teeth and tonsils have been vigorously attacked, the cancer in the meantime being overlooked.

7. The signs of advanced cancer of the tongue are too obvious to require discussion.

## CONCEALED CANCER OF THE TONGUE

Once an ulcerated or indurated area is discovered in the tongue of an adult man or woman, diagnosis should not long be delayed. The possibility of cancer should be seriously considered from the start and should not be dismissed until the lesion is proved not to be cancer. When doubt exists biopsy should be done, care being taken to include the margin of the lesion. A piece of sufficient size to insure good sections should be taken. The advantages of such a biopsy far outweigh the possibility of harm. The danger of dissemination of cancer of the tongue through a biopsy properly done has not been proven. Roux-Berger and Monod<sup>6</sup> state that biopsy has been done on 825 cases of cancer of the tongue at the Curie Institute without evidence of an aggravation of the disease.

If radical treatment of a lesion is under consideration, histological proof of its character should be established. Regaud<sup>7</sup> considers biopsy an indispensable part of the treatment of cancer of the tongue. He points out that it is no longer a manifestation of scientific curiosity, but rather an obligation on the part of the physician, and something which is due the patient. Clinical diagnosticians are sometimes wrong. In a little more than 5 per cent. of the cases reviewed, benign lesions, most often tuberculous ulcers, were mistaken for cancer.

Treatment of concealed cancer of the tongue does not differ in principle from that of cancer of the tongue in general except insofar as it may be influenced by the position of the tumor. Opinion is divided as to the relative merits of surgery and radium. Regardless of the agency used to destroy the local growth, however, any treatment of cancer of the tongue must include the regional lymph-nodes. This was emphasized years ago by Küttner.<sup>8</sup> The extent of adequate surgical treatment of cancer of the tongue has been logically presented in a recent work by Semken.<sup>9</sup> The radiological treatment has been fully described by Regaud,<sup>10</sup> Lacassagne,<sup>11</sup> Roux-Berger and Monod,<sup>12</sup> and, in this country, by Quick.<sup>13</sup>

Whatever treatment is elected must be thorough if it is to be effective. The first treatment is the decisive treatment. Recurrent cancer of the tongue, either local or in the regional lymph-nodes, is rarely cured by any method. The responsibility attached to the first treatment is considerable.

The prognosis in concealed cancer of the tongue is generally worse than that of the more obvious forms. This is not because of any biological peculiarity of the tumor but because late discovery and its usual proximity to structures adjacent to the tongue contribute to make it bad. The principal hope lies in earlier recognition and better treatment.

### SUMMARY

1. Cancer of the tongue in about 20 per cent. of the cases is anatomically situated in such a way that it escapes early detection.

2. Frequently, it is further obscured by the absence of symptoms, or by the presence of symptoms which are indirect and consequently liable to misinterpretation.

3. An attempt has been made to call attention to certain symptoms and signs which should suggest the possible presence of lingual cancer, and thereby lead to its earlier discovery.

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## TRAUMATIC PECTUS EXCAVATUM\*

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THE operative technics used in two cases of pectus excavatum are presented because there has not been, so far as I am aware, any previous report of operation performed for the traumatic chronic type of this deformity.

Trauma severe enough to fracture the flexibly suspended sternum is frequently fatal owing to this or associated injury. Malposition of fresh frac-



FIG. 1.—*Left*: Great depression of sternum and right ribs as a result of contraction in a chronic empyema in a child. *Right*: Symptomless pectus excavatum that patient believes has been present since birth (photograph shown through the courtesy of Dr. Reed Nesbit).

tures may be corrected by posture, traction through hooks or by open operation, but prevention of recurrence of deformity may be difficult because the fracture gives the constant in-pulling action of the normal negative intra-thoracic pressure an advantage which it does not possess when there is no break in continuity of the thoracic cage. A sprain of several sterno-chondral and costo-chondral joints without actual fracture of sternum, cartilages or

\* Read before the American Therapeutic Society, June 21, 1930.

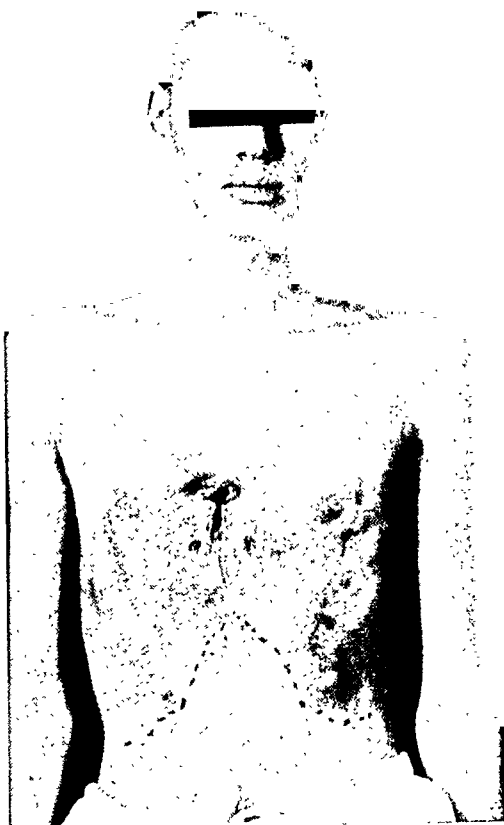


FIG. 2.—Case I. Before and after operation. The open wounds closed soon after photographs were taken.

## TRAUMATIC PECTUS EXCAVATUM

ribs gives the in-pulling action of the negative intra-thoracic pressure a similar, though perhaps, lesser advantage in causing abnormal depression of the sternum. So does rickets or the undue plasticity of the thoracic cage of some infants and youths. I now have as a patient a boy of twelve years of age with a great but symptomless depression of the sternum which is secondary to the fibrous contraction of a chronic tuberculous empyema (Fig. 1). Nageotte-Wilbouchewitch<sup>1</sup> found that 10 per cent. of 200 debilitated infants whom she studied showed inspiratory sinking in of the sternum.

The commonest type of pectus excavatum is the congenital (Fig. 1). In 1911 Ludwig Meyer<sup>2</sup> operated in such a case, resecting 2.5 centimetres of the

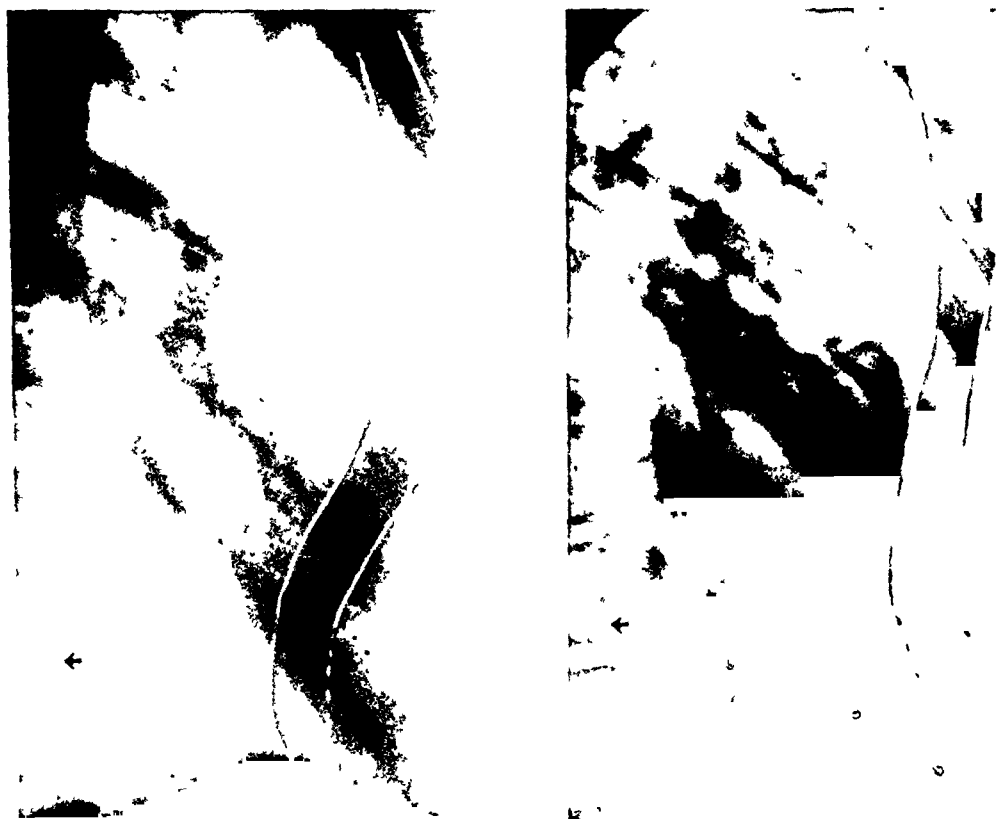


FIG 3.—Case I. Lateral roentgenograms before and after operation. The sternal outlines have been reinforced with pencil. Note proximity of sternum and spine before operation. The black arrows indicate the anterior surfaces of the vertebræ. (See Fig. 4)

second and third right costal cartilages; the patient was said to have lost his dyspnœa. Sauerbruch,<sup>3</sup> realizing that so incomplete an operation could not be expected to cure, resected 3 centimetre sections of the fifth to the ninth, inclusive, left costal cartilages and the left part of the sternum below the fourth cartilage. The patient was relieved of his dyspnœa and palpitation and was able to work from twelve to fourteen hours a day. In his second patient Sauerbruch resected the fourth to sixth left cartilages and the corresponding left half of the sternum and placed in the wound a fat graft from the thigh to protect the heart. The patient was relieved of dyspnœa and asthmatic attacks. Should symptoms recur, Sauerbruch would remove the



right costal cartilages but would leave the right half of the sternum. Hoffmeister<sup>4</sup> reports an operation by Lexer for congenital pectus excavatum in which the fifth to ninth cartilages on both sides were divided and the corresponding portion of the sternum dissected free. His intention was to turn over the concave sternum and replace it, but as there was a 1.5 centimetre gap between the divided ends of the cartilages on each side he removed the sternal piece.

It is a surprising but well-known fact that it is rare for even severe degrees of congenital pectus excavatum to present symptoms sufficiently troublesome even to suggest the use of surgery. Mild dyspnoea on exertion

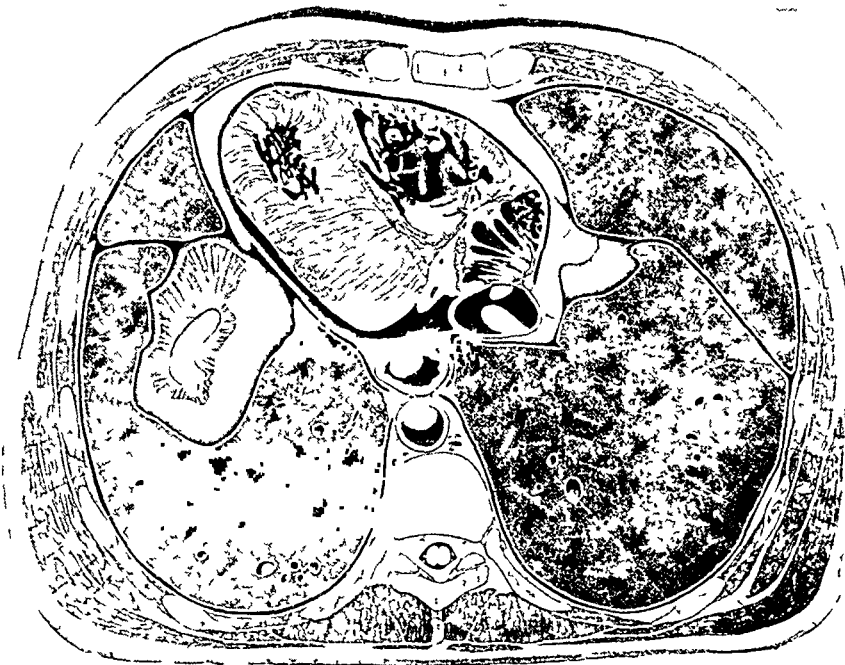


FIG 4.—Transverse section of a normal thorax through the fourth costal cartilages and eighth vertebral body. The compressing effect of such lessening of the distance between sternum and spine as exists in the pre operative röntgenograms of Figs 3 and 8 is apparent in this drawing (From Eycleshymer and Schoemaker A Cross Section Anatomy D Appleton and Co)

may be the only symptom. Pohl<sup>5</sup> has described an actual impression made upon the heart by a depressed sternum. In cases in which the sternum closely approaches the anterior surfaces of the vertebræ, the heart is often found to have been pushed entirely into the left hemithorax. Changes in the position of the heart have been discussed by Stadtmüller<sup>6</sup> and Rösler.<sup>7</sup>

Severe symptoms, when present, may be dyspnoea, agonizing oppression or pain in the cardiac region or referred therefrom, palpitation and disturbance of cardio-circulatory function. Occasionally patients are seen whose symptoms are sufficiently disturbing or disabling to require operation.

CASE I.—A boy of sixteen was referred by Dr. Nap Chaignon, of Port Austin, Michigan, and was admitted on July 17, 1929, to the University of Michigan Hospital complaining of increasing pain and depression in the sternal region. While wrestling four years before, his lower sternum was injured by heavy pressure. There was some

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pain, but not severe enough to require a physician; no deformity was noted at that time. The pain ceased but during the next three years the lower sternum gradually became depressed and during the last year the depression has progressed rather rapidly, and increasing local pain has caused him to stop work as a bellboy. There are now some dyspnoea and occasional dysphagia but no other gastro-intestinal nor cardio-circulatory symptoms.

Examination revealed a deep symmetrical depression of the lower half of the sternum and adjoining cartilages, the deepest point being opposite the end of the sixth cartilage (Figs. 2 and 3). The depression held 70 cubic centimetres. Respiratory movement was free at all levels. Both costal margins just mesial to the mid-clavicular lines were markedly buckled. The heart by percussion and röntgen ray was unenlarged but was displaced 3 centimetres to the left. Cardiac sounds and rate normal, pulses equal, blood

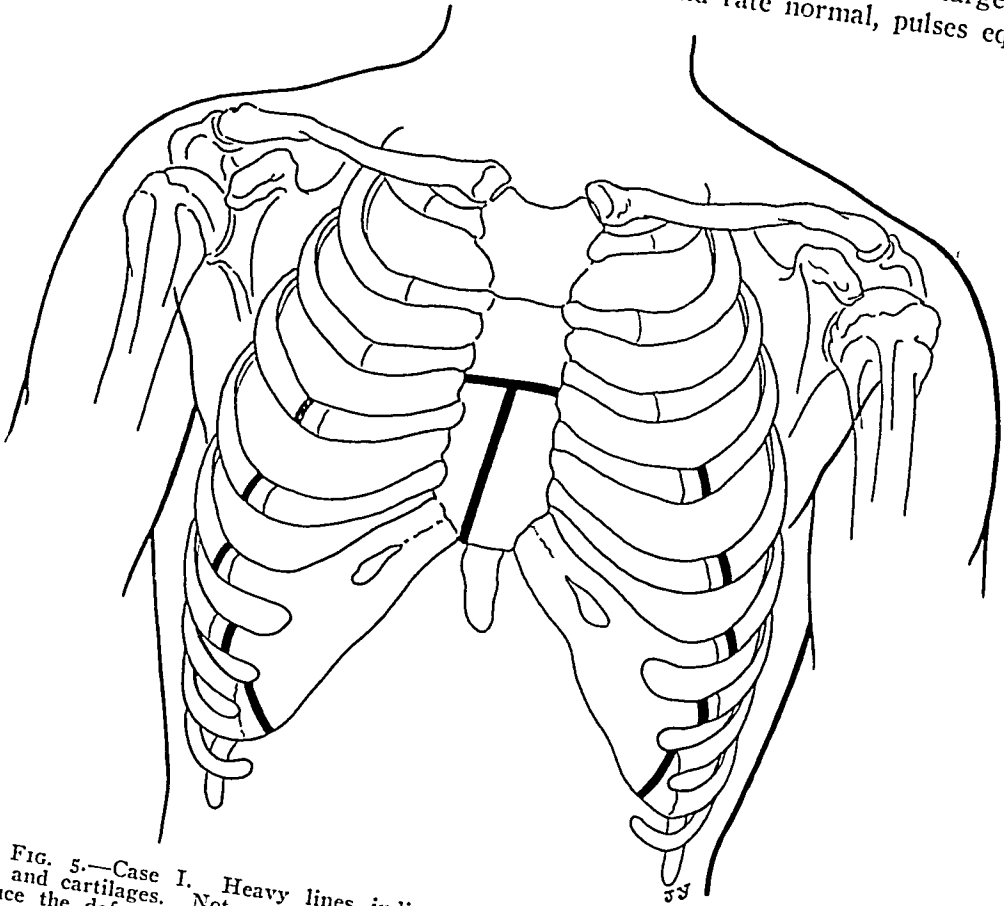


FIG. 5.—Case I. Heavy lines indicate places of operative division of sternum, ribs and cartilages. Not until all of these divisions had been made was it possible to reduce the deformity.

pressure 115/80, no cyanosis. The liver edge was 2 centimetres below the right costal margin. No abnormal pulmonary findings, no clubbing of fingers. A large barium-gelatin bougie passed freely through the oesophagus.

The progressive and disabling character of the pain and deformity seemed to justify an attempt at operative relief. On July 30 I operated (Fig. 5) under nitrous oxide anaesthesia. A short transverse incision was made over the sternum at the level of the third intercostal space and the sternum was transversely divided. A short incision was then made through the upper linea alba to the peritoneum and a finger was introduced through the interval between the right zipho-costal origins of the diaphragm to the posterior surface of the lower sternum; an attempt to lift it forward was without the least effect. Next, the fourth, fifth and sixth ribs were divided subperiosteally just lateral to their costo-chondral junctions, rather than through their cartilages, because actual bony union of these divisions was desired in order to make permanent the operative

reduction of the deformity. A further attempt to lift the sternum forward was fruitless. Next, the seventh, eighth and ninth cartilages of both sides were divided, and still the sternum could not be lifted forward. In view of this experience I do not understand how Zahradniček<sup>8</sup> obtained a satisfactory result in his case of an old pectus excavatum from merely exercising traction upon two wires introduced through operative perforations in the sternum.

Next, the sternum was divided longitudinally from the right of the xiphoid to the

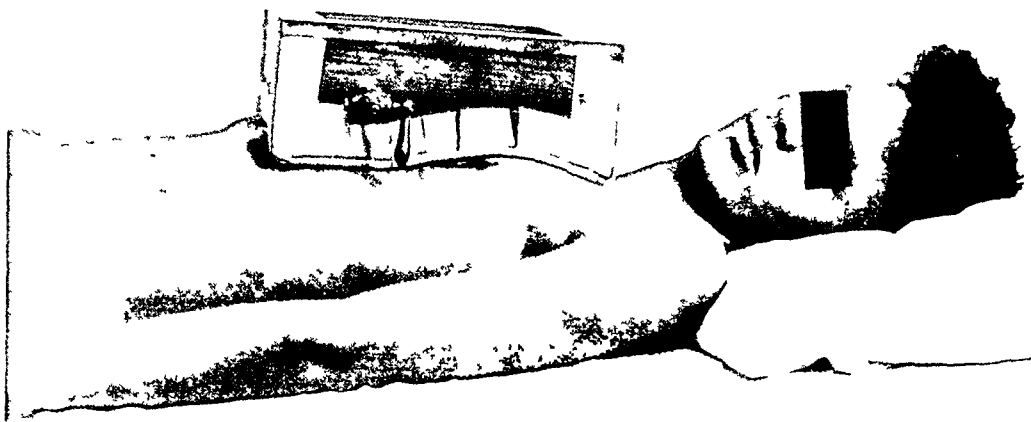
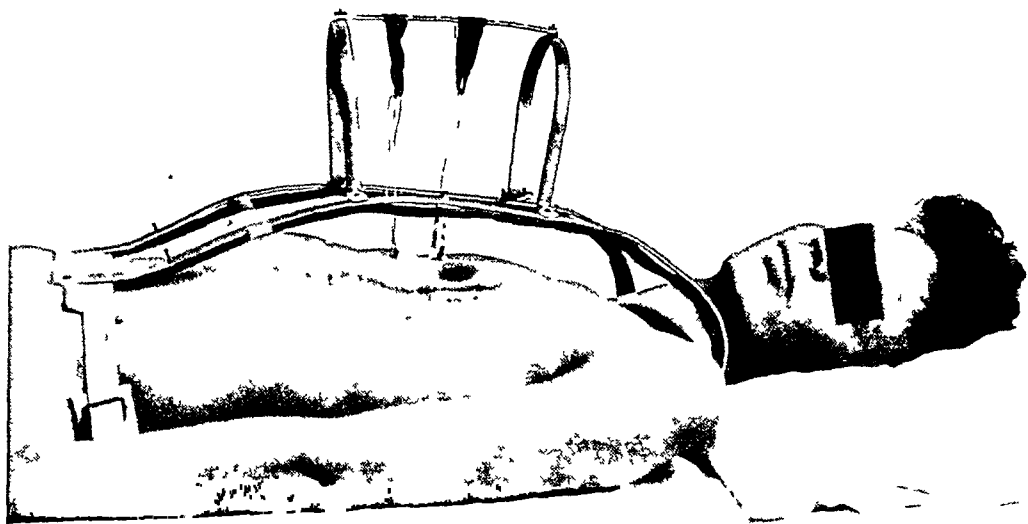


FIG 6—Case I *Above* Apparatus by which reduction of the sternal deformity was maintained for five weeks after operation. The band and wire surrounding the sternum are suspended to a bar by rubber bands. *Below* Box that was air tight with skin when negative pressure was created in it by connecting the pipe with the hospital air suction system. This box was used after removal of the apparatus pictured above in order to maintain reduction of the sternal deformity until firm bony union of the divided sternum and rib- occurred

place of transverse division and then a finger, introduced behind the sternum through the epigastric incision, was easily able to lift forward the sternum and its attached cartilages so that reduction of the deformity was complete

Throughout the operation care was taken not to separate the tissues of the anterior mediastinum from the sternum more than enough to admit the lifting finger. Wide

separation would have resulted, temporarily at least, in a large dead space after the sternum had been lifted forward.

A Parham fracture band and a silver wire were made to surround the sternum transversely, passing, respectively, through the mesial ends of the fifth and sixth intercostal spaces. The band and the wire were then attached to heavy rubber bands which in turn were suspended from a bar which was carried by a special apparatus† that had been fitted to the patient before operation (Fig. 6). Rubber bands were valuable in providing a "cushion" between the patient's tissues on the one hand and the movements of respiration and of the patient within his brace, on the other hand. Adjustment was made so as slightly to overcorrect the funnel-breast deformity thereby allowing for a tendency toward recurrence of the deformity under the physiologic influence that was discussed in the second paragraph of this article. The skin incisions were closed without drainage. At this time the blood pressure was 112/76 and the pulse 90; when the operation was begun they were 128/60 and 84. During division of one of the cartilages the pleura was torn. The resulting traumatic pleural effusion disappeared after two aspirations.

Ten days after operation the elastic traction of the rubber bands caused the sternum below the site of its transverse division to bulge forward and the sternal cutaneous incision to break down. This was remedied by adjustment of the traction. Thirty-five days after operation the lassoing band and wire were removed because of considerable fever, which rapidly became normal and the patient was discharged. The pain for which the operation had been performed disappeared completely from the time of operation.

Three months after operation the patient was seen again and a tendency to recurrence of the deformity was noted. Blow bottles were prescribed and for three weeks he intermittently wore an ingenious suction apparatus that was designed by my associate Dr. W. W. Buckingham (Fig. 6). This maintained the sternum in nearly normal position until its bony fixation seemed assured. Temperature normal, average pulse 80, respirations 20.

Ten months after operation the patient wrote that he has no pain nor dyspnoea even on exertion and that correction of the deformity is maintained.

CASE II.—A woman of twenty was referred by Dr. George H. Schroeder, of Chicago, on January 20, 1930, to the Medical Department of the University of Michigan Hospital in the care of Dr. Cyrus Sturgis, with whom I saw her in consultation. She complained of severe pains in the region of the heart, palpitation and dyspnoea. Two years before admission she was in an automobile wreck when she is said to have fractured her left clavicle and pelvis and dislocated her hip. She had not been told that her sternum was fractured. She was confined to bed for fifteen weeks and then walked to the doctor's office for examination, climbed the stairs, had an attack of palpitation, dyspnoea and pain in the chest, and "collapsed." Since this time the symptoms have become more and more severe. The pain is aggravated into what she terms "attacks" by even a short walk, excitement or nervousness and in these attacks she is apprehensive. The pain which is usually in the region of the apex of the heart and left axilla, is occasionally referred to the left shoulder but not down the arm. Recently, she says, there has been some slight swelling of the legs and ankles. During the past three months she has been unable to work as housemaid.

She states that when six years old she was confined to bed for five weeks with painful joints from which she entirely recovered. Seven years ago she experienced attacks of dizziness, palpitation and fainting which her doctor said were due to cardiac disease. In common with her parents and three brothers and sisters, she is subject to attacks of migraine.

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† This apparatus was designed and constructed by Mr. George E. Curry, Chief of the University Hospital Appliance Shop.

Since the occasion when she "collapsed" in the doctor's office after the accident, she has presented many manifestations of hysteria, consisting in attacks of tonic and clonic convulsions of the extremities and eyelids; blurring of vision; inability to speak; blueness and coldness of the fingers and lips; severe constipation with great distension.

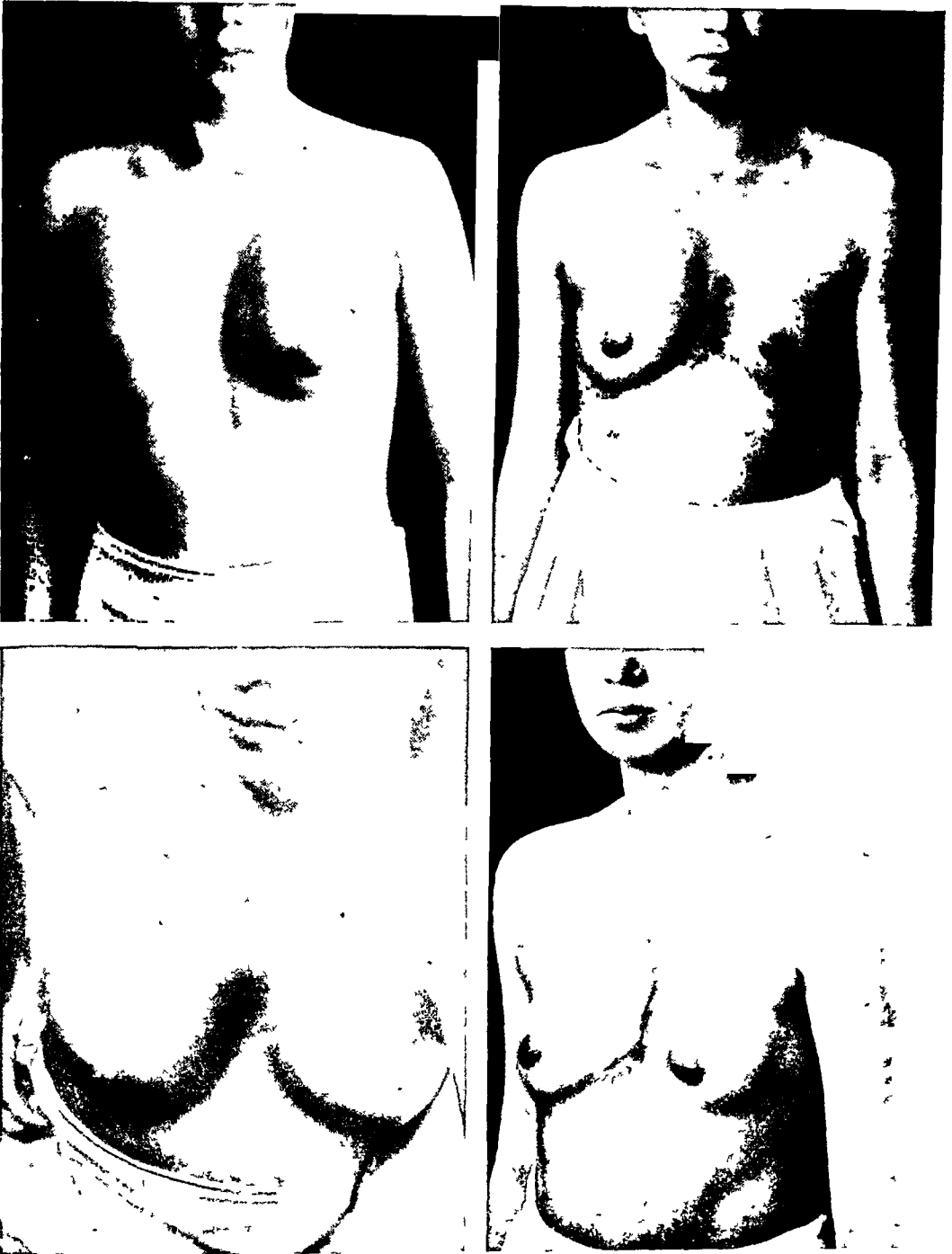


FIG 7—Case II. Before and after operation

At various times during her residence in the hospital she has complained mildly of pains almost everywhere in the body, but severely only of those at the heart. She states that the convulsive attacks usually succeed a marked aggravation of cardiac pain. She does not bite her tongue nor urinate during them. In one attack observed at this

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hospital the cardiac rate was 200 and there were rapid deep sighing respirations and tight voluntary closure of the eyes. Dr. Carl Camp, Department of Neurology, confirmed the diagnosis of hysteria.

Examination showed a deep symmetrical depression (Fig. 7) involving the gladiolus of the sternum and the third, fourth, fifth and sixth costal cartilages. The maximum depth of the depression was at the level of the fourth intercostal space. The lateral röntgen film (Fig. 8) showed a sternal fracture at the level of the fourth cartilage, the upper fragment being drawn back about 5 centimetres. The antero-posterior film showed a bulging of the heart in the region of the left auricle. The size and position of the heart were approximately normal, the pulse from 80 to 100, blood pressure 125/80. At the apex and extending toward the axilla there was in the recumbent position a soft systolic murmur which increased during inspiration. In the first and second left intercostal spaces near the sternum there was a short high-pitched systolic murmur, which



FIG. 8.—Case II. Lateral röntgenograms before and after operation. The white arrows indicate on the pre-operative print the sternum at the point of its greatest depression, and on the post-operative print the height to which the operative sternal resection was carried. The black arrows indicate the anterior surfaces of the vertebræ. (See Fig. 4.)

increased with inspiration, and a loud second sound. The murmurs were scarcely audible when the patient was sitting or leaning forward. There were no abnormal sounds in the tricuspid or aortic valve regions nor in the carotid or subclavian arteries. An electrocardiogram taken by Dr. Frank Wilson during one of her convulsive seizures, which began with marked increase in cardiac pain, showed only sinus arrhythmia and sinus tachycardia with an inverted T wave in lead 3 and flat in lead 2.

The feet and legs were cold. The lips, hands, feet and legs were slightly cyanotic but not œdematous. There were no abnormal pulmonary signs. The eye grounds were normal. No hyperæsthesia or paræsthesia but both conjunctivæ were anæsthetic. Physical examination otherwise was negative.

The patient was kept under observation and at rest by the Department of Internal Medicine for five weeks without noticeable improvement and after another five weeks at home the pain, if changed at all, was worse.

Whether or not surgery was indicated presented a delicate problem. The patient certainly had hysteria and as certainly she had suffered a grave injury from an accident that had immediately killed her fiancé who was in the seat next to her. We had direct evidence of encroachment upon the heart by the depressed sternum, and the murmur in the pulmonic valve area suggested the possibility of some depression of the anterior wall of the right ventricle. The cardiac pain was disabling and unrelieved by prolonged rest. The patient consented to operation (Fig. 9) which I performed on April 4, 1930, under nitrous oxide anæsthesia.

A gently curving incision was made from the left second intercostal space at the parasternal line to the sixth left cartilage and then across to the right border of the sternum. The fourth and fifth left costal cartilages were removed extraperiosteally and the fourth intercostal bundle and transversus sterni muscle divided and the pleura pushed

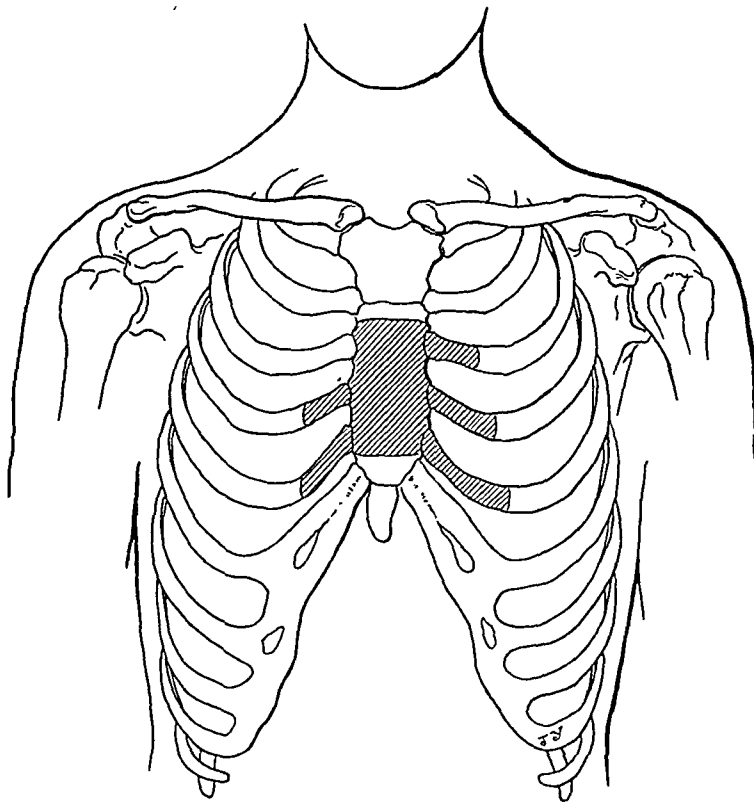


FIG. 9.—Case II. Shaded area indicates portions of sternum and cartilages removed at operation.

to the left. A finger introduced between the depressed sternum and the heart was tightly squeezed; after removing with the rongeurs the left half of the sternum between the second and sixth cartilages, the heart definitely bulged forward and the anæsthetist noted a marked improvement in the volume of the pulse. Then the entire width of the sternum with almost all of its periosteum was removed between the level of the sixth costal cartilages and just below the level of the second cartilages. The third left cartilage was now removed, as had been the fourth and fifth, to within 2 centimetres of their costo-chondral junctions and the mesial 2 centimetres of the fourth and fifth right cartilages were also removed (Fig. 10). The right pleura was torn and the lung was kept expanded by slightly raising the pressure of the anæsthetic gas being fed to the patient. The resulting skeletal defect measured 9 by 6 centimetres. The mesial edges of the pectoralis major muscles, which had been lifted on each side in order to resect cartilages, were sewn together without tension. The subcutaneous tissue, which was unusually thick, and the skin were sutured as separate layers.

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These continuous strong sheets of pectoral muscle (after operation, contraction of the pectoral muscles showed that they spanned the bony defect as a continuous sheet) and subcutaneous tissue, together with what bone might form from the fragments of periosteum that were not removed, seemed to promise adequate protection to the heart and against herniation of the heart and pulmonary borders. Such herniation is sometimes seen in congenital absence or cleft of the sternum (Greig<sup>9</sup>) but in these cases there is absence of the pectoral muscles in front of the defect, and only skin covers the pericardium. Should herniation have occurred in my patient I would have placed a grill of costal or cartilaginous strip grafts in the defect.

At the beginning of the operation the pulse was 116 and the blood pressure 125/85; at the end they were 92 and 108/80.

From the time of operation the cardiac, axillary, and left shoulder pain was no

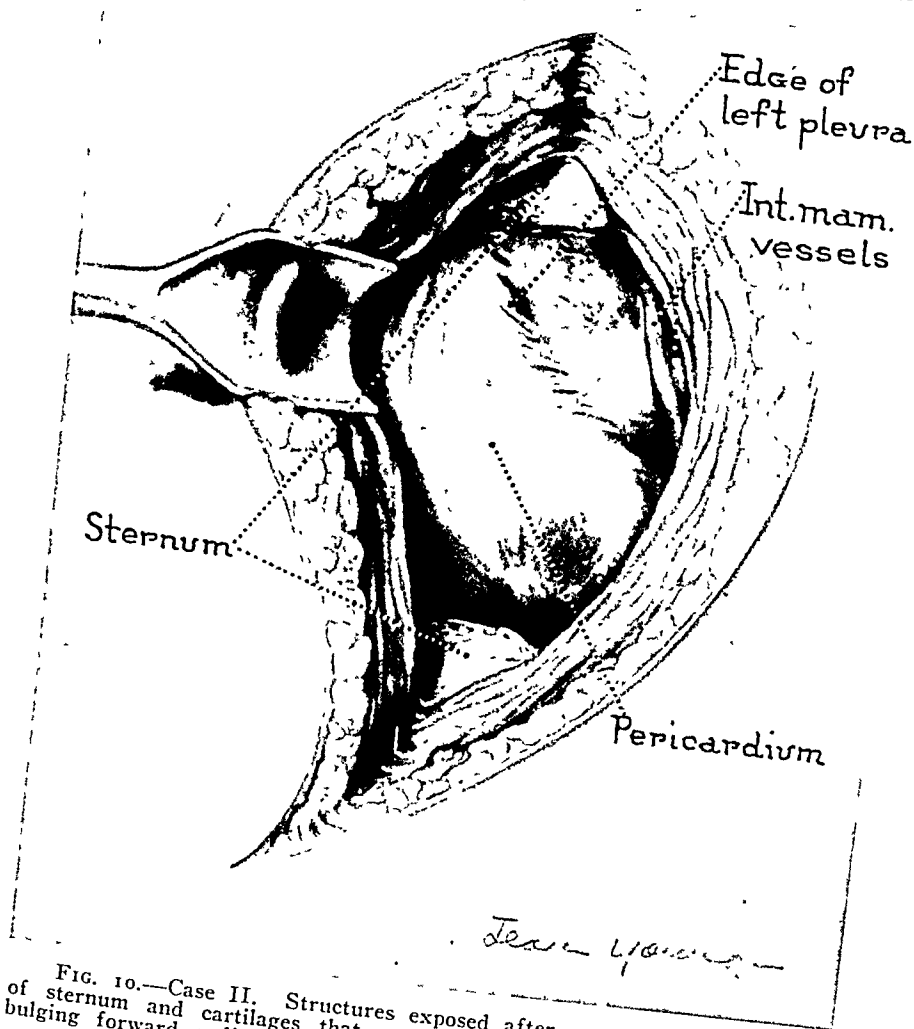


FIG. 10.—Case II. Structures exposed after removal of the portions of sternum and cartilages that are pictured in Fig. 9. The heart is bulging forward a little after its decompression.

more. After her operative convalescence she was accepted by the Department of Neurology for treatment of her continuing hysterical manifestations.

Before operation there was a respiratory expansion of 2.5 centimetres in the sagittal diameter of the thorax at the level of the greatest depth of the depression and after operation of 6 centimetres. After operation the antero-mesial ends of the cartilaginous stumps moved somewhat posteriorly during inspiration while the ribs at the mid-clavicular lines moved anteriorly.

At the time when these operations were performed I knew of no precedent and therefore devised technics which seemed suited to the individual



problems. In the first patient the defect was considerably broader than in the second and the resection type of operation might have entailed removal of greater lengths of the cartilages than would have been safe with respect to protection of the thoracic viscera. This factor was of slight additional importance because the patient was a male who might be expected to lead a more strenuous life than a woman, and who had no prominent breasts to serve as a buffer against trauma.

Operation in the first patient was certainly a far more extensive one than in the second, but it did not prove to be shocking and it did leave complete bony protection to the thoracic viscera. The second operation was far simpler to perform and its effective action did not depend upon a complicated and difficult maintenance of reduction of the deformity until firm bony union should have taken place. Also it was possible, although at operation the supposition was found to be false, that the frank fracture of the sternum, with its resulting callus, that had occurred in the second patient might have presented technical obstacles to the "unfolding" operation that was performed in the first patient. The loss of the bony covering of the heart seems to be of little consequence in the second patient for the reasons that I have given.

In neither case did the operation cause any detectable impairment of cardiac or respiratory function and in both the purposes for which operation was performed were fulfilled.

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# ACTINOMYCOSIS OF THE KIDNEY \*

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RENAL actinomycosis in the past has been considered as primary when the disease was confined to the kidney, and secondary when other actinomycotic lesions were associated in other structures of the body. It is difficult to conceive of the kidney as the site of a primary infection, and it would seem that involvement of the kidney, in most instances, if not in all, must be secondary to a portal of entry through mucous membrane. The kidney may become involved by direct extension from the gastro-intestinal tract in abdominal actinomycosis, through the diaphragm from pulmonary disease, or by metastasis through the lymphatics or blood-stream.

In the case herein reported, as nearly as can be determined, the disease was confined entirely to the right kidney, as is evidenced by the patient's complete recovery after right nephrectomy. However, that the condition may have been secondary to actinomycosis of the appendix must be given consideration, even though such infection was never proved in the appendix or intestinal tract, and even though there was no evidence that such infection ever had existed.

REPORT OF CASE.—A man, aged thirty-two years, an accountant, previous to July, 1928, had had repeated attacks of pain in the right lower quadrant of the abdomen. In July, 1928, he was operated on elsewhere than at the clinic, and a ruptured, partially gangrenous appendix was removed. Drains were inserted for three weeks; then the wound was allowed to heal. In six weeks, apparently after an uneventful recovery, he left the hospital with only a slight amount of serous drainage. This subsided and he gained in strength.

September 10, 1928, what was apparently a stitch abscess developed and was drained. The wound was packed for one week and finally healed. September 27, the patient felt feverish, had night sweats, lost appetite and pain developed in the right costovertebral angle. Examination revealed only a tender right kidney. The patient was hospitalized, symptoms continued, and vague distress developed in the right portion of the epigastrium. The urinary tract was normal on laboratory and cystoscopic examination. The condition grew worse. A mass, which seemed to be liver, became palpable and progressed downward; it was painful to pressure and movement. Chills, jaundice, or digestive disturbances other than a poor appetite were not present. There was less pain over the costovertebral space; the urine was clear; leucocytes numbered 16,000 in each cubic millimetre of blood. October 27 it was concluded that a retroperitoneal abscess was present. A small incision was made in the right upper quadrant of the abdomen, and after careful exploration only slight enlargement of the liver was found. The incision was closed without drainage and primary healing occurred.

February 25, 1929, a cold developed; the patient had a chill and ran an elevated temperature for ten days. He had another chill, following which he improved except for residual discomfort in the right kidney. April 4 the symptoms and signs of October,

\* Read before the American Association of Genito-Urinary Surgeons, May 22, 1930.

1928, were exactly reproduced except that this time the amount of pus in the urine was increased.

May 16, 1929, the patient registered at The Mayo Clinic. He weighed 115 pounds, which, according to him, represented a loss of twenty-five pounds. His skin was tanned but he was anæmic, graded 2, and his tongue was furred. He had moderate tenderness in the right costovertebral angle, and resistance in the right upper half of the abdomen.

In the hospital he ran a septic temperature varying between 102.5° and 97.3° F. In roöntgenograms there was a large right renal shadow and absence of the outline of the psoas muscle. The urine repeatedly contained pus, graded 3. Leucocytes numbered 13,000 in each cubic millimetre of blood. The concentration of hæmoglobin was 30 per cent. In a test of renal function with phenolsulphonephthalein 80 per cent. of the dye was returned. The Wassermann reaction of the blood was negative. The concentration of



FIG. 1.—Elongation of upper and lower calices, suggesting tumor.

urea was eighteen milligrams in each 100 cubic centimetres of blood. A right pyelogram, May 20, showed that the pelvis was small, and that there were several small filling defects. The upper and lower calices were elongated and the middle calices were absent. The upper minor calix was dilated. The ureter was normal. The pyelogram suggested a right renal tumor, with marked decrease in function and marked infection of the kidney. (Fig. 1.) The left kidney was normal in function.

May 24, right nephrectomy was done. The kidney was one and a half times normal size and was densely adherent as a result of old perinephritic abscess, which, although large, had pretty well subsided. What appeared to be a carbuncle measured eight, six and four centimetres in various diameters and involved the middle third of the renal substance. The pathologic report was of multiple confluent abscesses involving the cortex and medulla of the central portion of the kidney; so-called carbuncle of the kidney; marked perinephritis, with old perinephritic abscess, and destruction of about 70 per cent. of the renal substance. (Figs. 2 and 3.)

July 3, nearly six weeks after operation, a diagnosis of actinomycosis was made through recovery of actinomyces from the wound. The wound, at this time, consisted of multiple deep sinuses, and in order to carry out adequate therapeutic measures for actinomycosis, the wound was widely opened to the bottom of all sinuses and was packed wide open with gauze. Intensive treatment with röntgen-rays and with the use of radium in the depths of the wound was instituted. Iodides were given in the form of a 10 per cent. solution of sodium iodide intravenously, and potassium iodide by mouth. The patient was dismissed December 2, 1929, with a practically completely healed wound and with return of normal weight and strength. It has not been possible, at any time, to find lesions elsewhere in the body which might be considered to be those of actinomycosis. Repeated röntgenologic examination of the thorax failed to reveal any evidence of pulmonary involvement.

Within two weeks we have had a report on the patient's condition. Complete healing of the wound has occurred, and the patient is entirely well.

*Comment.*—If the original classification of actinomycosis of the kidney must be adhered to, this case may well be considered one of primary acti-



FIG. 2.—External surface of kidney.



FIG. 3.—Extensive involvement of kidney.

nomycosis with recovery subsequent to nephrectomy. Israel was the first to report a case of primary renal actinomycosis. At the time the report was made, in 1901, the patient had remained well eleven years after nephrectomy. The same author in 1911 reported a second case, with recovery after nephrectomy. Since that time Stanton, Kunitz, Kleinschmidt, Pinner, Bevan, Abbot, Peacock, Christison and Warwick, and Beregoff have each added one case. Von Lichtenberg stated in his "Handbuch der Urologie" that primary renal actinomycosis had been reported only seven times; Von Lichtenberg included, as did Abbot, a case reported by Theodore Cohn and one by Earl. Data available did not seem sufficient for us to include Cohn's case as one of true renal actinomycosis. Data in Earl's case are lacking beyond the statement that the patient was a male, aged fifty-two years, in whom a secondary actinomycotic abscess of the brain was found.

The case reported by Christison and Warwick can hardly be considered one of renal actinomycosis, for only the suprarenal gland was involved and that secondarily to pulmonary actinomycosis in which the infection had traversed the diaphragm.

The kidney is sometimes involved secondarily as a part of generalized actinomycosis. Von Lichtenberg stated that secondary actinomycosis of the kidney occurred in nine of 128 fatal cases of actinomycosis in which necropsy had been done, an incidence of 7 per cent. In all but one of these nine cases both kidneys were involved. Pinner stated that in 460 cases of actinomycosis of the thorax and abdomen there were sixteen in which the kidney was involved secondarily.

Objective and subjective data concerning the urinary tract and suggesting renal tumor or infection of the kidney in the presence of actinomycosis else-

TABULATION  
*Summary of cases of renal actinomycosis from literature*

| Author                 | Age, years | Sex | Pre-operative diagnosis or basis for diagnosis | Operation or necropsy | Observations at necropsy  | Results             |
|------------------------|------------|-----|--|-----------------------|---|---------------------|
| *Israel                | 33         | M   | Actinomyces from sinus                         | Nephrectomy           |   | Recovery            |
| *Israel                | 60         | F   | Perinephritis                                  | Nephrectomy           |   | Recovery            |
| *Stanton               | 53         | M   | ?  | Necropsy              | Actinomycosis confined to right kidney  | Death               |
| *Kunith                | 5          | M   | ?  | Nephrectomy           |   | Recovery            |
| Kleinschmidt           | 24         | M   | Renal tumor                                    | Nephrectomy           |   | Unknown             |
| *Pinner                | 40         | M   | Actinomyces found in urine                     | Nephrectomy           |   | Recovery            |
| Bevan                  | ?          | M   | ?  | Drainage              |   | Unknown             |
| Abbot                  | 43         | F   | Renal tumor                                    | Drainage              | Perinephritic abscess; destruction of two vertebræ; multiple actinomycosis of lungs | Death in two months |
| Peacock                | 8          | M   | Renal tuberculosis                             | Nephrectomy           | Actinomycosis of liver  | Death               |
| Christison and Warwick | 8          | M   | ?  | Necropsy              | Extensive actinomycosis of lungs and involvement of right suprarenal gland          | Death               |
| Beregoff               | 63         | F   | Actinomyces found in urine                     | Necropsy              | Bilateral renal actinomycosis   | Death               |
| *Hunt                  | 32         | M   | Renal tumor                                    | Nephrectomy           |   | Recovery            |

\* Apparently true cases of primary renal actinomycosis.

where, or history of preëxisting actinomycosis perhaps should cause one to think of this type of renal involvement. However, unless actinomyces are present in the urine or in a post-operative sinus, there is little to suggest a pre-operative diagnosis of renal actinomycosis. In the cases reported in the literature it is of interest that actinomyces were found in the urine of two patients (Pinner's and Beregoff's) and this led to the clinical diagnosis of renal actinomycosis. In several instances, the diagnosis was established through the finding of actinomyces in material from a sinus which persisted after drainage of a perinephritic abscess or which persisted subsequent to nephrectomy. In three cases, including our case, a pre-operative diagnosis of renal tumor had been made.

In seven of the twelve cases in the literature, including our case, nephrectomy was done. Five patients recovered. The result in Kleinschmidt's case, in which nephrectomy was done, is not recorded. Death occurred on the twelfth day in Peacock's case in which nephrectomy had been done, and actinomycosis of the liver was found at necropsy.

The prognosis in actinomycosis in general is notoriously poor. Recovery from so-called primary renal actinomycosis, when the disease is confined to one kidney, may be expected only by means of nephrectomy and the institution of therapeutic measures such as those which are employed for actinomycosis in other situations. These measures were used in the case reported and are, in brief, the following: (1) maintaining the wound wide open to its most dependent parts; (2) packing the wound wide open, down to its lowest depth, with gauze saturated with dichloramine-T in 4 per cent. solution, or with compound solution of iodine (Lugol's solution) diluted to one-third to one-half strength; (3) introducing radium into the wound as long as sulphur bodies are repeatedly found; (4) administering treatment by röntgen-rays over the entire area, and (5) persisting in the use of iodides in the form of a 10 per cent. solution of sodium iodide intravenously, or the oral administration of potassium iodide, or both.

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# ENUCLEABLE MULTILOCULAR ABSCESS (CARBUNCLE) OF THE KIDNEY\*

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Two cases have, in large measure, furnished the basis for the above title. Their records will be used as an introduction to a brief discussion of the treatment of a relatively uncommon renal condition.

CASE I.—A man, twenty-four years of age, admitted to the Surgical Service of the University of Virginia Hospital, May 19, 1923, had had diffuse abdominal pain, malaise and fever for six days. Significant physical findings were lacking. During three days' observation, his temperature ranged between  $103^{\circ}$  and  $106^{\circ}$ , pulse around 90, leucocytes were 6000, urine showed a few pus-cells. He was then transferred to the Medical Service with a tentative diagnosis of typhoid fever.

There, repeated blood cultures, stool cultures and serological tests did not reveal a typhoid or paratyphoid infection. He slowly developed localized discomfort and tenderness in the right flank, ultimately presenting, just below the rib margin, a rounded mass moving with respiration. Coincidentally, the temperature chart exhibited a septic curve, the leucocyte count mounted to 17,000. June 25 he was transferred to the Urological Service.

Both kidney urines were pus-free, cultures negative. Thirty-minute phthalein output after intravenous injection was 16 per cent. on the right, 12 per cent. on the left, no bladder leakage. Right pyelogram was normal but the renal shadow was abnormally large. A working diagnosis was made of renal abscess or perinephritic abscess, or both. At operation, June 27, the posterior perirenal tissues were soft, the kidney itself about twice normal size, intensely congested. As it was being freed intracapsularly, pus pockets were entered in a prominent area on the anterior surface of the middle third. By mere chance, my finger found a line of cleavage about a localized suppurative mass and readily enucleated it. The resulting depression had a diameter of about five centimetres, and a depth of two centimetres. Its wall was smooth and appeared healthy. Save for the marked congestion, the remainder of the kidney seemed normal. A two-ounce perinephritic abscess medial to the kidney had evidently followed erosion of the capsule overlying the conglomerate renal abscess. Thorough drainage was established and the wound loosely closed. *Staphylococcus aureus* was grown from the pus. (A later account was secured of a few boils antedating onset of illness by a month.)

*Pathological report.*—Dr. W. E. Bray. "Specimen is an irregular mass 6 by 4 by 2 centimetres, rather firm, containing many small gray abscesses and a few large ones. Microscopic sections show kidney tissue with degenerated tubular epithelium. The tubules are separated by rather large amounts of young fibrous tissue in which are many deeply staining round cells and plasma cells, as well as p. m. n. s. Here and there are miliary and larger abscesses with areas of necrosis. Some abscesses have considerable fibrous tissue in their walls. There is some necrosis near the edge of one section, but this does not suggest an infarct. *Diagnosis.*—Acute purulent inflammation with abscesses; chronic inflammation."

The patient was discharged well thirty-seven days after operation.

CASE II.—A man, twenty-nine years of age, admitted August 27, 1924, had suffered from recurrent, severe, left renal colic for seventeen days, afebrile for the first twelve days,

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\* Read before the American Association of Genito-Urinary Surgeons, May 22, 1930.

thereafter with chills and fever. I first saw him September 1. Temperature then was 104°, leucocytes 13,000, the urine pus-laden. There was slight tenderness in the left flank, no induration. He presented an extensive Vincent's gingivitis, a sternal periostitis, an effusion in the left knee, a positive blood culture (*staphylococcus aureus*). Urinary tract films were negative. Cystoscopic investigation had shown the left urine very purulent, the right clear, the left fifteen-minute phthalein output 0, the right 8 per cent. Ureteral catheter drainage of the left pelvis had been established.

The sternal infection went on to a frank *staphylococcus osteomyelitis*, resulting ultimately in the loss of two-thirds of this bone. The gingivitis was controlled after three weeks of vigorous treatment. Blood cultures were positive through September 6.

Cystoscopic findings September 19 were as before, both kidney cultures positive (*staphylococcus aureus*). There was slight pain and tenderness in the left flank, no induration.

A small stone was found in the bladder September 29. This had no doubt come from the left ureter though neither X-ray examination nor repeated ureteral catheterization had suggested its presence. The left urine still contained much pus, but phthalein output (fifteen-minute intravenous) had risen to 6 per cent. against 11 per cent. on the right. Save for slight fuzziness of outline, the left pyelogram appeared normal.

October 4 abscesses of the prostate and soft tissues over the left shoulder were drained. By October 10 there was induration both in the left costo-vertebral angle and deep-seated in front below the kidney region. Temperature continued to have a daily maximum of 102° to 103°. The kidney was explored that date with a working diagnosis of pyelonephritis and perinephritic abscess. The perinephritic tissues were very thick and œdematous. About five ounces of pus were evacuated from an abscess below the lower pole. The true renal capsule was exposed, opened and gently separated from the kidney. On the anterior surface of the upper one-third a group of abscesses was thus demonstrated. Since the feel and appearance here called to mind the previous case, a line of cleavage was sought and found. A septic mass approximately five to six centimetres in diameter was readily enucleated. It had a clean-cut line of demarcation from the surrounding kidney and seemed to have a very definite capsule. While the kidney was large and very hyperæmic, neither palpation nor inspection gave evidence of other abscesses. The kidney, therefore, was not removed.

*Pathological report.*—Dr. W. E. Bray: "Carbuncle-like mass measuring about 5½ by 3½ by 3½ centimetres, surrounded, save where ruptured, by a thin glistening capsule. Cross-section shows discrete abscesses of varying size, all containing thick greenish-yellow pus. Microscopic sections show acute suppurative inflammation of the kidney with multiple abscesses. One edge of the section is smooth and covered chiefly with fibrin and blood, along with some purulent exudate. No definite old fibrous capsule is made out, but there is an incomplete peripheral layer of young granulation tissue (early stage of encapsulation)."

His general condition promptly improved markedly. The daily temperature maximum shortly dropped to 100°. Seventeen days after operation the left kidney urine was grossly clear, sediment showed six to eight pus-cells to the high power field, culture was still positive. Phthalein output was 11 per cent. on the right, 6 per cent. on the left. Three days later, October 30, his temperature suddenly jumped to 104° and remained at that level. Careful overhauling revealed no new development to account for the change. It was decided that further suppuration in the left kidney was the most probable cause. For this reason, a nephrectomy was done November 3. "The kidney measured 15 by 6 centimetres. The surface is smooth except near the upper and middle thirds where there is a depression at the site of the former operation. The kidney is firm and the cut surface is apparently normal except for a few small yellowish opaque areas suggesting fatty degeneration. *Microscopic.*—One section shows almost complete loss of normal structure, being chiefly inflammatory tissue with œdema, hæmorrhage, and cellular infiltration. Another section shows dilated tubules with degenerated and desquamated epithelium and a number of hyalin casts, also purulent exudate in a few tubules. The



section through base of operative depression shows hæmorrhage, œdema and infiltration with round cell, p. m. n. s. and a few giant cells. There is considerable young fibrous tissue superficially and hyalinization of deeper fibrous tissue. Shortly after the nephrectomy a right pneumonia was demonstrated, this followed by a streptococcus empyema. Death occurred November 8. An autopsy was not permitted.

The localized inflammatory process above described obviously warrants the title multilocular abscess and, further I think, fulfills all the requirements of the lesion first called renal carbuncle by Israel in 1891. Objection is raised from time to time to applying the term carbuncle to the kidney on the ground of definitional incompatibility or of adding further complexity to the classification of renal infections. While there is sound logic in this, the vivid descriptive value of the word, together with the sanction of increasing international usage, has doubtless secured for it a permanent place in medical terminology. It must be remembered, however, that the renal carbuncle of many writers is the infarct, septic infarct, multiple abscess, conglomerate abscess, or abscess of others.

The carbuncle in Israel's first patient was so sharply defined in color and consistency from the surrounding uninvolved kidney tissue as to give the impression of an imbedded tumor. Subsequent writers have often emphasized similar striking demarcation by verbal description and sometimes by accompanying illustrations. (Horn, Reschke, Barth, Nicholich, Hotchkiss.) In Fisher's case the carbuncle was actually sequestered. Barth and Smirnow in particular refer to the rich increase of connective tissue found about the pus pockets. An occasional illustration (Dick) suggests a thick fibrous tissue layer encircling the whole mass.

Other authors speak of the carbuncle shading off imperceptibly into the adjacent renal tissue. Frequently the carbuncle bulges above the cortical surface and has developed more at the expense of the cortex than the medulla. It may, however, be quite deep-seated and of an extent to cause demonstrable compression of a calyx or calices, even of the pelvic body. Infrequently there may be two lesions in the same kidney (Smirnow, Eisendrath).

The carbuncle now and then is reported as having broken down to practically a single abscess cavity. It has not always been clear to me how cases found in the abscess stage and cured by drainage have justified report as carbuncles. Smirnow concludes that renal carbuncle has no tendency to such breaking down and will not accept as carbuncles large solitary abscesses so reported. I would deem it perfectly possible for a renal carbuncle to soften down to a solitary abscess but, so found, the evolution is hard to prove.

In a series of fifty-seven cases collected from the literature, the following final methods of treatment have been employed: primary nephrectomy twenty-eight times with two deaths; incision and drainage eleven times with two deaths; secondary nephrectomy eight times with one death; primary excision six times with no deaths; secondary excision twice with no deaths; and enucleation twice with no deaths. The nephrectomies totaled thirty-six with three deaths; other operations twenty-one with two deaths.

The figures indicate the decided necessity of, or preference for, nephrectomy as the surest and safest form of treatment. The extent of the process in many of the cases so handled clearly would have made a less radical procedure foolhardy. The illness of the patient sometimes has led to removal of the kidney even though the carbuncle seemed resectible (Barth). One would certainly expect nephrectomy to secure the smoothest convalescence, particularly if there is no complicating perinephritic abscess. Even the strongest advocates of primary conservative operations state that a later nephrectomy may be required.

Israel considers resection to be peculiarly suitable and feasible for renal carbuncle. He mentions the potential danger of thus leaving unrecognized foci but believes such may well be taken care of by the body once the chief suppurative lesion is removed. Reschke successfully utilized excision three times and is a forceful advocate of conservative surgery for the condition. One of his excision cases developed an abscess in the same kidney during convalescence but this was readily drained through the original wound. Barth employed excision once with a good result and expresses the belief that he could readily have done so again in place of a nephrectomy. Nicholich voices a similar feeling in discussing the sharp demarcation of the carbuncle in a removed kidney. Successful resections are recorded by Lennander, Blum (cited by Israel), von Herczel (cited by Voss). Most writers mention resection as a possibility where the carbuncle is small, early, or sharply delimited, but actually the method seems to have been used quite infrequently. Where employed, incisions have been carried into the surrounding healthy tissue and the carbuncle extirpated in one or more pieces.

The only cases I found handled by enucleation are two reported as having infarcts by Hotchkiss in 1913. In the first, in addition to a perirenal abscess and an abscess of the upper pole, "there was found also a considerable triangular area of soft, white infarction, apparently riddled with small abscesses, and measuring about two inches across its base and not extending into the pelvis . . . infarcted portion readily enucleable with finger . . . was neatly extirpated in this manner . . . the walls of the triangular gap in the kidney looked to be covered with granulations." Recovery followed. His second case showed a small perinephritic abscess. "There was a good-sized white infarct in the upper pole of the organ, which was riddled with small abscesses. As the rest of the organ appeared uninvolved, the whole area including the infarct was easily enucleated with the finger and without any considerable bleeding as the wall of the gap in the kidney appeared to be granulating, and healthy."

The enucleation in my first case was entirely unpremeditated and followed upon my finger finding an unexpected line of cleavage as the extent of the carbuncle was being explored. In both cases the enucleation was as easy as is the shelling out of a fibromyoma from the uterus. The second specimen grossly had a very definite glistening white capsule. Such was not observed for the first case, though the demarcation from the surrounding renal tissues was equally sharp in both instances.

I am convinced that the secondary nephrectomy in Case II was quite unnecessary. The gross and microscopical appearance of the kidney suggested that it was recovering well from the unusual combination of an obstructive pyelonephritis and a carbuncle. The wisdom of having done

a nephrectomy shortly after admission is another question but not pertinent to the topic under discussion.

Conservative surgery for renal carbuncle gains considerable support from an analysis of the twenty-one cases so treated—removal ten, incision and drainage eleven—in the series of fifty-seven reviewed. No secondary nephrectomies were necessary. Autopsies on the two patients who died, four days and twenty-four hours, respectively, after drainage of a carbuncle, revealed thrombosis of the iliacs and vena cava in one and an unsuspected carbuncle in the second kidney in the other.

The rare occurrence of bilateral involvement must be kept in mind in deciding upon the operative involvement for a given patient. Kretschmer has reported one such case, Smirnow cites two (Stuckey, Rjasanzewa). Reschke recounts the autopsy demonstration of a carbuncle in one kidney and an abscess in the other. The problem for the surgeon is much simpler, confronted later with a suppurative lesion in the second kidney, if the original carbuncle has permitted handling by some method less radical than nephrectomy.

I have no means of estimating how often enucleation will be possible for renal carbuncle. I feel it will occasionally prove a practical method where an excision, or, more particularly, a nephrectomy might otherwise be done. The paucity of reference to the procedure in the literature has seemed to justify giving it some attention. Certainly, when feasible, it is ideally conservative.

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# INDICATIONS AND TECHNIC OF COMBINED URETERONEPHRECTOMY\*

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A REVIEW of the progress made in reno-ureteral surgery since the first nephrectomy was performed by Simon in 1868 reveals that very little attention has been given to the variety of pathological lesions that involve the surgical ureter and necessitate its complete removal.

The intention of this presentation is, therefore, to focus the attention, particularly of specialist surgeons, upon the various problems that oftentimes arise after nephrectomy, when an infected ureter stump has been left behind. It is also my purpose to point out the convenience and the importance, whenever there is a definite lesion of the ureter that requires such a radical procedure, of the two-stage aseptic operation for the excision of the entire ureter and kidney in one piece and at one sitting; namely, a total ureteronephrectomy, as in the case of a young patient on whom I performed it, a few months ago, with a curative and successful result.

It must be remembered, however, that most authors have always accepted the idea that the remaining portion of the iliopelvic ureter ligated at the lower pole of the kidney and left behind after a lumbar nephrectomy becomes functionless and atrophic and is gradually reduced to a fibrous thin cord of aberrant tissue without further significance as a potential site or cause of further trouble.

Moreover, studies upon the normal ureter after nephrectomy, both by animal experimentation and clinical observation, have led to the conclusion that the ureter loses its rhythmic contractions and becomes obliterated in a period of from nine months to three years, by gradual and marked atrophy of its muscular coat. Although this assertion must be granted as regards the evolution of the normal ureter, the case is otherwise with abnormal infected ureters which present hazards. It seems right to emphasize that when the pathological condition involving the kidney has invaded the walls of the ureters, and caused marked ureteritis with nodular infiltration and peri-ureteritis or hypertrophic hydro-ureter or pyro-ureter, if this is not removed in its entire length at the time of nephrectomy, surprising trouble is liable to arise from the infected stump of the ureter. This occurs more times than the urologist cares to remember, as I have found in a survey of the literature, and has been in many instances, and in fact in my own practice, the cause of persistent urinary disturbances, which after long suffering and the use of various methods of treatment fail to obtain cure and ultimately

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\*Read before the Section of Genito-urinary Surgery, New York Academy of Medicine, May 21, 1930.

necessitate a subsequent ureterectomy. In other words, the usual complications of what should have been a curative nephrectomy are manifested clinically by a long delay in the healing of the wound, with persisting uropurulent lumbar fistula, marked pyuria, hæmaturia, tumor and stone formation, with colic pain in the abdomino-inguinal region, bladder tenesmus and frequent desire to urinate—symptoms which obviously call for excision of the infected stump ureter by a secondary operative procedure that is difficult to perform owing to the condition of septic ureter and the formation of scar tissue and dense adhesions to the walls of the peritoneum and surrounding structures of the lower pelvis.

Not until recent years with the development of pyelography, ureterography and cystography has it perhaps ever been possible to recognize the clinical and anatomopathological entity with perfect accuracy in the diagnosis, before performing a surgical intervention upon this duct, whose main function is none other than that of conveying the urine from the kidney to the bladder. The routine method of urological examination nowadays is so essential that no operation upon the organs of the upper urinary tract can be practically justified without the assurance of a sound prognosis such as can be obtained only by the brilliant methods which are now available in modern urography.

Several conservative operations are performed upon the ureters, but at the present time I will discuss only the indications and technic of a total ureteronephrectomy obviating the necessity of a secondary ureterectomy in the attempt to relieve symptoms and to produce a permanent cure. I shall, therefore, briefly review the literature on the subject and the different methods of technic employed, and will finally attempt to illustrate my paper with the report of two personal cases which I was so fortunate as to handle with success and which have been the basis of this study.

These two cases represent the two most common types of surgical problems to be encountered in routine practice. The first is a case of nephrectomy for atrophic, hollow kidney, without function, secondary to multiple stone long impacted in the pelvic ureter, which necessitated, four months later, a subsequent ureterectomy for the infected stump of the ureter, in order to cure a permanent lumbo-abdominal fistula. The second illustrative case, in a girl seventeen years old, with a long history of disturbances in which the pyelo-ureterogram revealed a megalo-ureter or hydropyo-ureteronephrosis with complete loss of function, is one in which I did a two-stage aseptic ureteronephrectomy in one sitting, ending with an uneventful recovery. The operation, while appearing to be a formidable one, is, in reality, quite safe and does not affect the patient more than any other simple surgical procedure.

#### HISTORY AND LITERATURE

Operations upon the urinary tract, particularly for the removal of stone or to drain pus cavities, are known to have been performed since the time of

Fig. 1.—Case I. Röntgenogram with catheter and instrument in position, showing shadow of multiple primary calculi impacted in the sacroiliac pelvic portion of the left ureter of long standing, causing obstruction to normal drainage and making the catheterization of the ureter impossible.



Fig. 2.—Case I. Pyeloureterogram of same case, revealing a peculiarly shaped point where the previous shadow indicated the impression of an atrophic hollow function-ureter, preventing the normal outflow.



This case illustrated the convenience of primary ureteronephrectomy.

Hippocrates and the earliest days of medical science, but the operation for a complete excision of ureter and kidney, whenever it is indicated, is a relatively recent achievement of modern urology.

In fact, the first ureterectomy ever performed appears to have been carried out by Reynier, in 1892, on a patient who needed three consecutive operations, for the removal of an infected ureter stump left behind at the time of nephrectomy for pyonephrosis. Reynier's case is fully described in



FIG. 3.—Case I. The same patient who came back to the clinic two months later, after nephrectomy and incomplete ureterectomy, complaining of uropurulent abdominal lumbar fistula due to the infected ureter stump which contained a calculus. The ureterogram reveals the injected sodium iodide coming out from the ureter to the skin, necessitating a secondary ureterectomy to obtain cure.

Rousseau's Paris thesis published in 1893. It appears that the patient had a very stormy convalescence, necessitating the three subsequent operations that were performed at different times afterward by the lumbar, sacral and inguinal routes, ending finally with the successful accomplishment of a total ureterectomy which served, I think, to open a new era for the pathological conditions of the surgical ureter.

One year later, Poncet, in a case of renal tuberculosis, thoroughly de-

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scribed in Riaudet's theses, confirmed the value of the excision of the entire length of the ureter whenever the tuberculous process has definitely involved the ureter. The case was that of a nephrostomy for a tuberculous pyonephrosis, which necessitated a secondary nephrectomy and, two and one-half years later, a total ureterectomy for a permanent lumbar sinus that apparently refused to heal even after curetting and other palliative treatments, and which undoubtedly was due to the tuberculous ureteritis of the infected ureter stump.

But it is to Howard Kelly that most of the credit must go for having performed, December 18, 1895, the first total nephro-ureterectomy in a patient twenty-three years old, suffering with reno-ureteral tuberculosis, with surprising curative results. Mention must also be made of Albarran, who, in 1898, performed ureteronephrectomy in a case of multiple papillomatous growth of the bladder, ureter and kidney pelvis, in one sitting removing the entire ureter and kidney with complete recovery of the patient. Both operations were performed retroperitoneally and by the long lumbo-ilioinguinal route of incision, with complete success.

However, this operative procedure did not gain in popularity during those early days, one reason for this being the lack of facilities for obtaining correct diagnosis and consequently proper indications.

Nevertheless, as progress has continued to grow with the perfection of cystoscopy, catheterization of the ureters, the renal function test and the use of röntgenography, the clinical conception has become more clear to the surgeons for the diagnosis of lesions involving the ureter, and even before urography was put into practice, more progress in the operative treatment of the ureter appeared to be made.

Kelly, Montgomery, Pozzy, Bovee, Noble and other gynecologists began to advocate the combined abdomino-vaginal route, first described by Kelly in 1896 for the total excision of the kidney and ureter simultaneously in cases of renal tuberculosis with pathological ureter. But this procedure, while difficult for lack of vaginal exposure at the fundus of Douglas's cul-de-sac and because of the damage it inflicted in opening the peritoneum, was promptly discontinued and later the same authors gave more attention to the previous method already described above. The purpose of this operation as performed by Kelly was to avoid the extensive cutting of the abdominal wall to divide the shock and facilitate the combined procedure by removing the vesical end of the ureter through the vagina. While good in technic, it is perhaps difficult to practice and is, of course, applicable only in the female.

Israel, Albarran, Kelly and others, therefore, were using in these days the most commonly known, long, lumbo-abdominal, extraperitoneal incision of exposure, which ran from the twelfth rib at the costovertebral angle obliquely down toward the ilioinguinal region and to the semilunar line about an inch above the symphysis pubis, cutting all layers of muscles so as to expose the whole kidney and ureter. Sometimes he started the operation from above downwards, and sometimes from below upwards, according to



the convenience of the case and with the purpose of removing the kidney and ureter *in toto*. But while good results apparently were obtained, one cannot fail to admit that such an enormous incision across the belly's wall appears altogether too drastic and may perhaps cause a weakening of the abdominal wall's resistance, perhaps resulting later on in an abdominal hernia, which patients hesitate to permit.

Later on, Hartman, Kelly, Albarran and Lilienthal, in 1911, called attention to the convenience of the two-stage combined incision of exposure by the lumbar and inguinal route for accomplishing the nephro-ureterectomy, but the procedure did not come really into vogue until Edwin Beer, in 1921, and Judd, Papin, Young, Joly, Kidd, Hunt and others reported cases, and again called attention to its convenience and the importance of its use.

After Beer's presentation, with the report of several cases without death or complications, many surgeons employed the combined method of technic in the two-stage ureteronephrectomy, serving for the removal of the entire ureter and kidney in one piece without opening, and commencing with the first step of the operation from below, cutting the ureter from behind the bladder as in the case that I am about to describe.

It is a well-recognized fact nowadays that the pathological ureter must be excised at the time of nephrectomy as low down as possible, but when the diagnosis of the lesion involving the ureter has been previously made, the operation is best handled commencing from below. In other cases when the diagnosis is not a perfectly clear proposition, the surgeon will do better to commence from the kidney and explore downwards, then make the second incision at the external border of the rectus muscle or at the inguino-abdominal region parallel to Poupart's ligament according to his preference, cutting the ureter behind the bladder between a double ligature, extra-peritoneally, in order that the kidney and ureter after blunt dissection may be pulled from above and removed *in toto*.

Although this complication of the ureter stump clinically appears to be rather common, it is surprising how few text-books have even mentioned or discussed the importance of this surgical problem. Therefore, pre-operatively, it should always be recognized that in many cases the indications for a primary total ureteronephrectomy deserve consideration as well as those for a subsequent ureterectomy and that the total extirpation in one sitting should be practiced more often than is the case today.

In the last two decades the literature of this subject has been very scarce. Besides the names already mentioned there are two important contributions worth mentioning: one, that of Henri Lorin, of the Necker Clinic, published in 1913, on the rôle of the ureter after nephrectomy, and the other, that of Raymond Lathem, in 1922, from the Mayo Clinic. Both papers are experimental and clinical studies revealing the pathogenesis of the infected ureter stump as the cause of pus and infection and calling attention to this common occurrence.

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More recently a few other interesting articles of great clinical significance have enriched the literature on the subject, among which the names of Frank Kidd, Thomson Walker and Verne C. Hunt are worthy of mention.

*Indications for ureteronephrectomy.*—Since I have been studying the etiology and pathology of vesico-renal reflux in a paper that I had the honor to present before this section in December, 1928, and later before the meeting of the American Urological Association, held at Vancouver, B. C., in July,

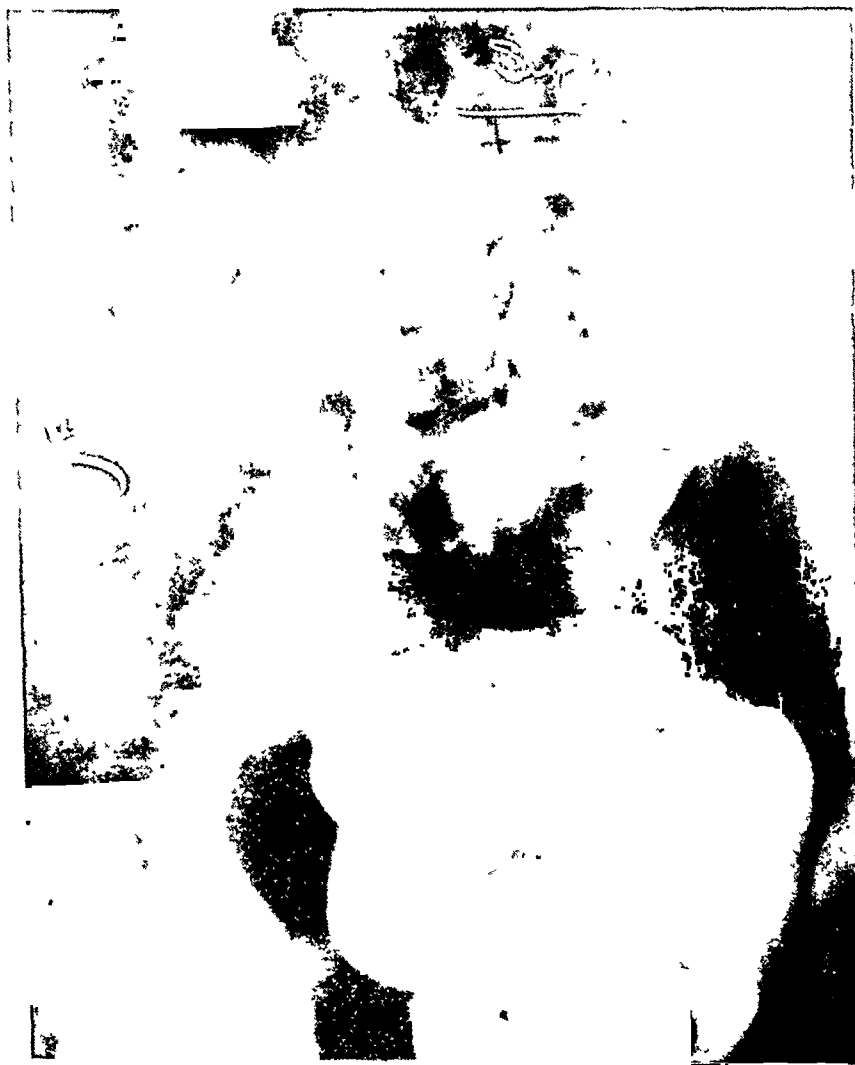


FIG. 4.—This is the cystogram of a man thirty years of age which revealed hydroureter and hydronephrosis of the right side. With the presence of tubercle bacilli in the urine, this gave evidence of a right tuberculous kidney, for which ureteronephrectomy is indicated. However, the patient did not return to the clinic and no further data were obtained.

1929, I have come to the conclusion that much overlooked pathology of the surgical ureter and kidney is at the bottom of the necessity for this radical operative treatment.

In that paper I thoroughly discussed the value of cystography, and the congenital and acquired type of vesico-renal reflux. I also called attention to the fact that, when the kidney on one side has lost its function causing hydro-ureter and hydronephrosis, ureteronephrectomy is the only curative treatment available to the urologist, and that in many instances, when the

ureter has been transplanted to another portion of the bladder, reflux of the vesical contents occurs and the kidney gradually becomes pyonephrotic, necessitating, in many instances, its complete removal to relieve pain and symptoms.

TABLE I

*Indications for Ureteronephrectomy, versus nephro-ureterectomy*

1. In hydronephrosis, simple or infected, where the stricture is low down in the pelvic ureter or in the intramural portion of the vesical ureter.

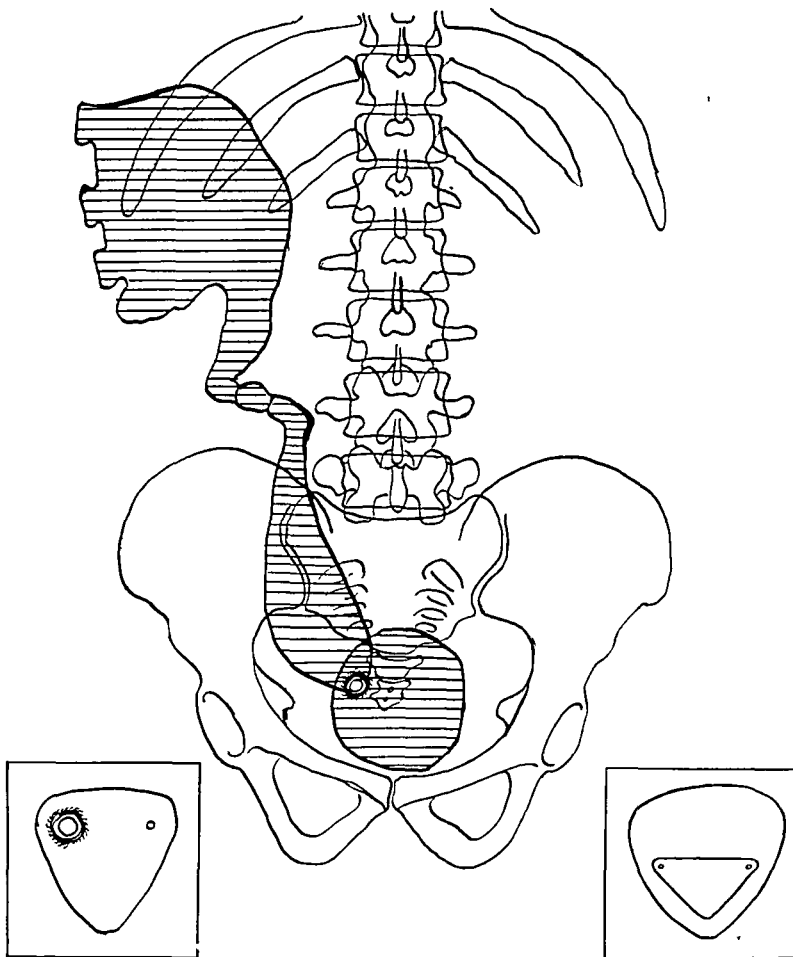


FIG. 5.—A drawing of the same case showing the cystoscopic finding of a patulous and greatly dilated "golf hole" type of ureteral orifice on the right side, the left ureteral orifice being normal. Here cystography confirmed the diagnosis of vesico-renal reflux, in which type of case, when unilateral, the combined primary ureteronephrectomy is well indicated.

2. In pyonephrosis or atrophic, hollow, septic or aseptic kidney secondary to a stone long impacted in the pelvic ureter.
3. In tuberculous pyonephrosis associated with marked ureteritis and peri-ureteritis, or definite involvement of the ueter, as in megalo-ureter and rosary-tuberculous ureter.
4. In all other types of pyonephrosis associated with fibrosis or dense inflammatory stricture low down in the pelvic ureter.
5. In cases of vesico-renal reflux with hydro-ureter and hydronephrosis, when unilateral, as:

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- a. In gaping or "golf hole" ureteral orifice due to congenital malformation.
- b. In ureteroneocystostomy when resulting in vesico-uretero-renal reflux.
- c. In persisting vesico-uretero-renal reflux after prostatectomy.
- d. After meatotomy for an impacted stone in the intramural vesical portion of the ureter when causing reflux and ascending infection.
- e. When the ureter opens into a bladder diverticulum and there is no sphincter action at the mouth of the ureteral orifice, giving place to ureterocele formation with definite back pressure, ascending infection and reflux.
- f. When the ureter has been transplanted to another portion of the bladder, resulting in vesico-renal reflux and a functionless organ.



FIG. 6.—Cystogram of a patient who had a ureterocystoneostomy ten years ago for malignant growth of the intravesical portion of the ureter, which it has never been possible to catheterize. In combination with urinary symptoms the cystogram revealed vesico-renal reflux with hydroureter and hydronephrosis such as almost always occurs in cases of transplantation of the ureter to another portion of the bladder, requiring the combined ureteronephrectomy (Lowsley's case).

6. In papilloma of the renal pelvis, ureter and bladder.
7. In primary carcinoma of the ureter.
8. In congenital ectopic ureter opening extravasically as in the wall of the vagina associated with congenital cystic or atrophic kidney.
9. Infected ectopic pelvic kidney with pathological ureter.
10. For stone long impacted in the lower portion of the ureter, causing complete obstruction and distortion of the whole kidney parenchyma.

11. Heminephrectomy for horseshoe kidney or duplication of pelvis and ureter, when associated with stone impacted low down in the pelvic ureter.
12. In leucoplakia of renal pelvis and ureter.
13. Primary fibro-fatty ureteritis, tuberculous or otherwise, where infection has extensively damaged the wall of the ueter, yet has left the kidney comparatively free
14. In persisting ureteral vaginal or rectal fistula with pyelonephritic infection, and when all other palliative measures fail to obtain cure.
15. When the ureter has been transplanted to the rectum and ascending infection has developed, as could be revealed by intravenous pyelography.



FIG 7—Pyeloureterogram revealing filling defect of multiple papillomatosis of kidney pelvis and upper ureter, indicating the convenience of total ureteronephrectomy

Many other types of lesions call for the veritable necessity of this radical two-stage procedure, but at this time I will not go into complete details in view of the limited time allowed for this presentation. However, while studying the subject, I have made two tables showing, in résumé form, what are the indications when the two-stage aseptic operation for ureteronephrectomy should be recommended, as I have performed it in one sitting with the most satisfactory results, removing the total specimen in one piece and without opening, thereby preventing contamination of infection. Both

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wounds of the operation healed firmly without incidents and a perfect curative result was finally attained. (See Figs. 17, 18, 19 and 20.)

Also, for practical purposes, I call attention in the second table to the incidental and true indications of a secondary ureterectomy, which I illustrate here-with in the report of my first case. (See Figs. 1, 2 and 3.)

TABLE II

### *Indications for secondary ureterectomy*

1. In infected stump of ureter due to tuberculous ureteritis and peri-ureteritis after a long period of medical and urological treatment when the cystitis and other bladder symptoms have not subsided.
2. In persisting uropurulent lumbar fistula when due to septic ureter stump and the presence of vesico-ureteral reflux.
3. In infected stump of ureter without drainage forming pyo-ureter or empyema.
4. In the presence of stone or foreign bodies in the ureter stump.
5. In cases of secondary papilloma implanted in the walls of the ureter stump.
6. In subsequent epithelioma of the ureter causing persisting painless hæmaturia.
7. In carcinoma of the remaining portion of the ureter after nephrectomy for renal neoplasm, and with recurrence in the intramural portion of the ureter and bladder.
8. When the cystogram reveals the presence of diverticulosis of the stump of the ureter, particularly if the diverticulum formation of the ureter is of the retentive type.
9. When the indwelling ureteral cathether and the lavage with antiseptic solution of the infected stump does not relieve the pyuria, "ureteric colic" and bladder symptoms of the aggravating condition.

It is obvious that in urinary surgery the diseases most commonly encountered in routine practice are urinary lithiasis, renal tuberculosis and malignant lesions of the bladder, ureter and kidney. There is also the rôle of infection of the upper urinary tract due to bacteria, urinary stasis and congenital malformation, such as gaping ureter, stricture of the intramural vesical portion of the ureter and abnormal extravesical supernumerary opening of the urinary duct, which, in many instances, causes the loss of its function, necessitating its complete removal. Up to the present time only the review of the literature will serve to reveal the paramount importance of these conditions that rela-

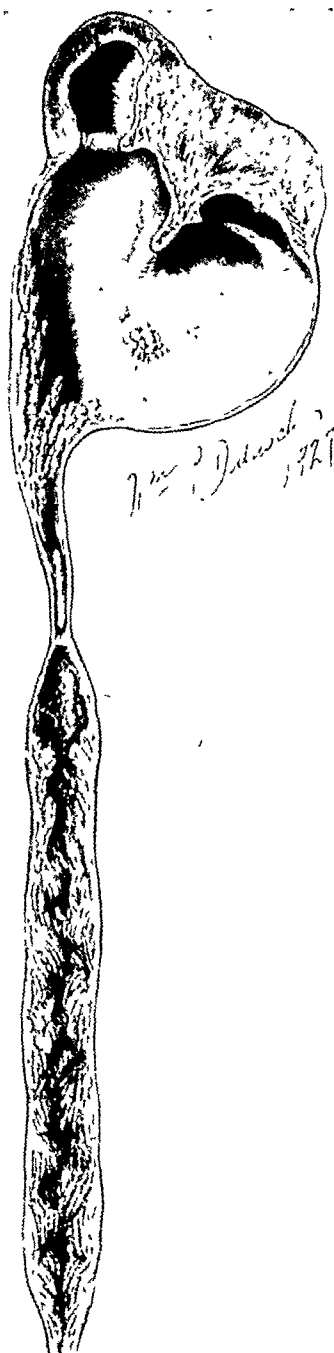


FIG. 8.—Drawing of a specimen showing hydro-nephrosis and huge diffused papillomatous growth of the entire lumen of the ureter, including the intravesical portion, which was removed in toto by nephroureterectomy. (Courtesy of Guyon Museum, of the Necker Hospital, Paris.)

tively commonly occur as a sequel to not having performed a uretero-nephrectomy at the beginning, or having done an incomplete nephro-ureterectomy.

Rafin, Poussou, Ferron, Sampson, Carraro, Legueu and Papin have called attention to the persistence of lumbar fistula after nephrectomy for renal tuberculosis in cases of vesico-renal reflux or well-advanced tuberculous ureteritis. The persistency of pyuria, pyo-ureter and marked bladder symptoms after nephrectomy have been well emphasized in the cases reported by Albarran, Israel, Escart, Rochet, Hyman, Read, Fowler, Fraustem and others. Stone formation or a stone left behind in the pelvic ureteral



FIG 9—Patient is a woman thirty-four years of age, who had her right kidney removed elsewhere. After persisting pain on the right side for more than three years and other urinary symptoms, a plain roentgenogram with ureteric catheters in position disclosed the presence of a stone about the size of an olive, in the right ureter stump at the brim of the pelvis, which was presumably left behind at the time of nephrectomy.

stump is of rather common occurrence, as has been recently discussed by Kidd and Hunt and as I illustrate in this paper with the report of Case I, and the radiogram of Doctor Lowsley's case, in which a secondary ureterectomy was done to attain curative results.

In many instances the undesirable complications of common occurrence in a nephrectomized tuberculous kidney are mainly due to the involvement of the ureter as well as the bladder and surrounding structures, but frequently to the fatty capsule and to contamination of the muscular walls of the wound, together with marked tuberculous ureteritis and peri-ureteritis; so that even when the ureter is divided by the thermocautery and ligated as

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low down as possible, often the wound breaks through, the stump of the ureter loses its ligature, and starts to discharge both pus and urine through the lumbar end—which condition is known to be the most annoying complication for delaying the healing of the wound and preventing the clearing up of the bladder symptoms (which, indeed, are responsible for the frustration of what should have been an uneventful nephrectomy). Many of these very important points and observations are discussed in contributions by Albarran, Mayo, Papin, Kretschmer, Judd, Scholl, Rafin, Böcmel, Walters, Marion and other writers, thus showing that a total ureteronephrectomy is the operative procedure of choice.

Primary malignant lesions of the ureters are extremely rare. Albarran and Imbert tabulated sixty-five cases of papillary epithelioma of both the ureter and the renal pelvis, and of these only thirteen were cases of primary cancer of the ureter. Kretschner, in reviewing primary carcinoma of the ureter, in 1924, counted thirty-five cases, and reported one case of his own. Moreover, Verne Hunt recently discussed two cases from the Mayo Clinic and stated that of fifteen cases of papillary epithelioma of the renal pelvis, nine came back after nephrectomy complaining of hæmaturia from the ureter stump, due to recurrence or secondary extension of the primary lesion of the renal pelvis to the infected ureter, which necessitated secondary ureterectomy. Hunt further said, "The best prognosis may be offered when the radical operation of nephro-ureterectomy, including the intramural portion of the bladder, is done immediately after the diagnosis of papillary epithelioma of the renal pelvis is established." Therefore, as Beer also stated, when there is evidence of a pathological ureter, a combined aseptic ureteronephrectomy should always be the operation of choice, so as to avoid metastasis, hæmaturia or recurrence of the tumor or other symptoms which end in the necessity of a secondary ureterectomy.

Another condition in which this radical two-stage operation is indicated is in congenital malformation where the authors and specialist surgeons are not entirely in accord as to the best method of treatment. In cases of congenital stricture of the pelvic ureter at the intramural vesical portion, causing urinary stasis of long standing with megalo-ureter or hydro-ureter and hydro-



FIG. 10.—Specimen removed at operation of previous case, showing the shadow of the stone in the portion of the stump of the ureter removed by secondary ureterectomy with satisfactory results.



nephrosis with complete loss of function, clearly revealed by the pyeloureterogram (as in Case II, which I am here reporting), and with infection, tuberculous or otherwise, ureteronephrectomy in two stages and at one sitting is the ideal operative method of treatment.

The problem of the extravesimal opening of a supernumerary ureter, while relatively rare, is of interest. Raymond Dossot, of the Necker Clinic, has collected and tabulated from the literature 154 unusual cases, ninety-five of which occurred in females and forty-six in males, with the sex not stated in the other thirteen, in which urinary incontinence, pus and infection have been noticed from birth. The supernumerary extravesimal ureter opened in

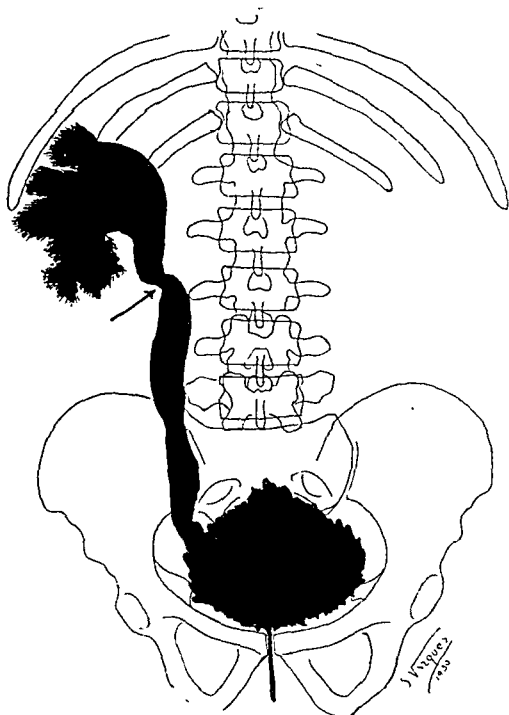


FIG. 11.—This drawing represents the incident of vesico-renal-reflux in urinary surgery, pointing to the convenience of primary ureteronephrectomy, particularly for renal tuberculosis, in order to avoid lumbar fistula and the other common complications observed after nephrectomy, when the ureter is ligated at the level of the lower pole of the kidney leaving behind an infected ureter stump.

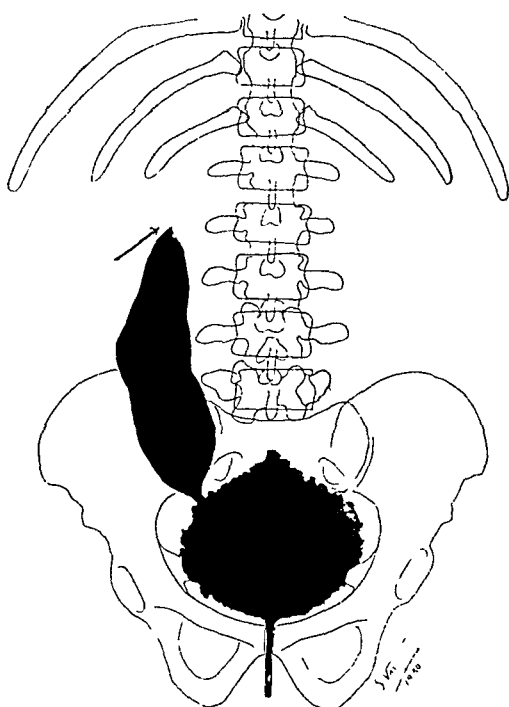


FIG. 12.—Illustrates the incident of diverticulosis formation of the ureter after nephrectomy in a case of vesico-renal-reflux of the retentive type, in which secondary ureterectomy is indicated.

the vulva forty-six times, in the urethra twenty-eight times and in the vagina fourteen times. While all these cases had been treated in different ways, many had been operated upon three and four times with consequent failure, recourse being ultimately had to nephrectomy and partial secondary ureterectomy.

Clinical experience, however, has shown that these ectopic, supernumerary or single ureters are always markedly dilated and without sphincter action at the point of their insertion, and as an evident result of this, the kidney tissue drained by them is always more or less injured and of no value physiologically. Therefore, their total removal by ureteronephrectomy is the

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only logical procedure. In some instances of a double kidney the good ureter or the one that opens normally in the bladder should be catheterized, and if there is good renal function, the catheter should be left *in situ* at the time of resection or of conservative ureteroheminephrectomy, which should be the operation of choice. Illustrative cases of this type have been reported by Albarran, Judd, Papin, Alessandri, Kidd, Furniss and other writers.

The importance of a secondary ureterectomy for the extirpation of the ureter stump left behind after the primary nephrectomy, which is, in many instances, as I have already shown, a complication of the same, needs no further emphasis at this time beyond the statement that complete removal of the ureter by total ureterectomy is justified, whenever it is diseased.

*Pre-operative measures and the anæsthetic.*—It is perfectly obvious that the case suitable for a combined ureteronephrectomy should receive the same care and attention as one for an ordinary nephrectomy, assuring, therefore, a good prognosis with the compensative renal function of the opposite side. The diagnosis must be accurate and conclusive of a functionless kidney with a clear-cut or definite lesion low in the pelvic ureter. Ureterograms and cystograms such as we make today are essential, and sometimes intravenous pyclography, when the ureter cannot be catheterized, is of real value in the pre-operative diagnosis. In other words, the surgeon must adopt the painstaking aphorism of "To plan what to do, or rather to know what to plan." Finally, before the operation the patient should be cystoscoped and an indwelling ureteral catheter fixed *in situ* in the ureter to serve as a guide to the surgeon so that he may readily locate and expose the ureter during the surgical procedure.

The anæsthesia to be employed is another problem of vital importance, particularly to patients who present poor risks due to weakness and long-standing infection, as in renal tuberculosis, or even when there is a slight

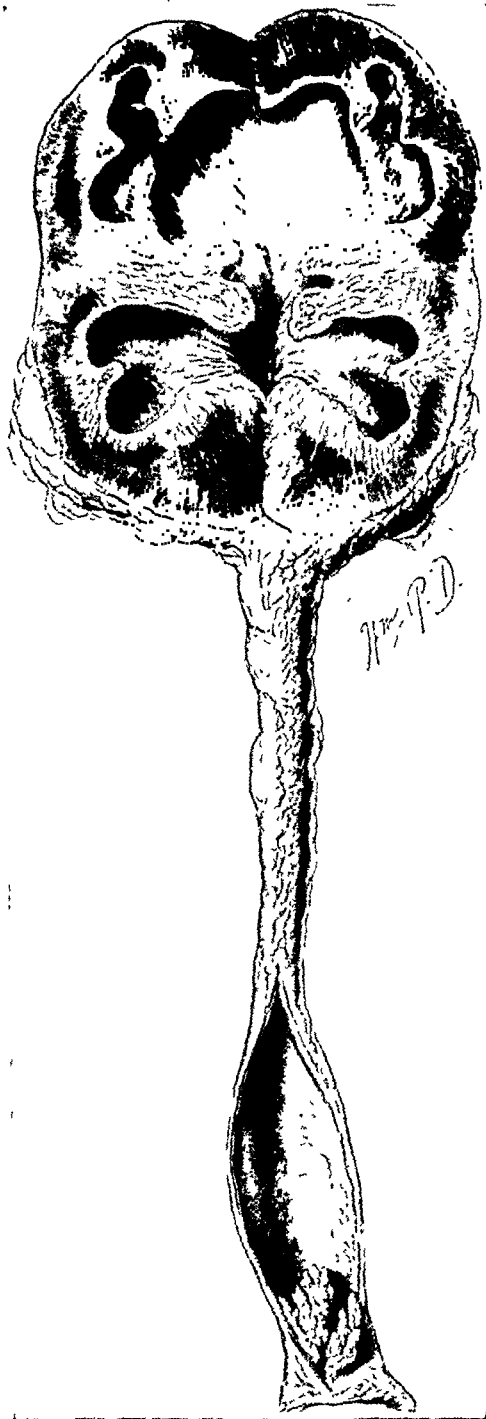


FIG. 13.—Drawing illustrates a case of primary malignant growth of the ureter removed by nephroureterectomy and shows the necessity of its total removal. (Courtesy of Guyon Museum, of the Necker Hospital, Paris.)

impairment of renal function in the opposite kidney. At the New York Hospital we have been using the paravertebral and also block method of infiltration with a solution of procaine 1 per cent. with satisfactory results. The first step of the operation can be performed with local anæsthesia, the second part being accomplished through the lumbar incision, when the

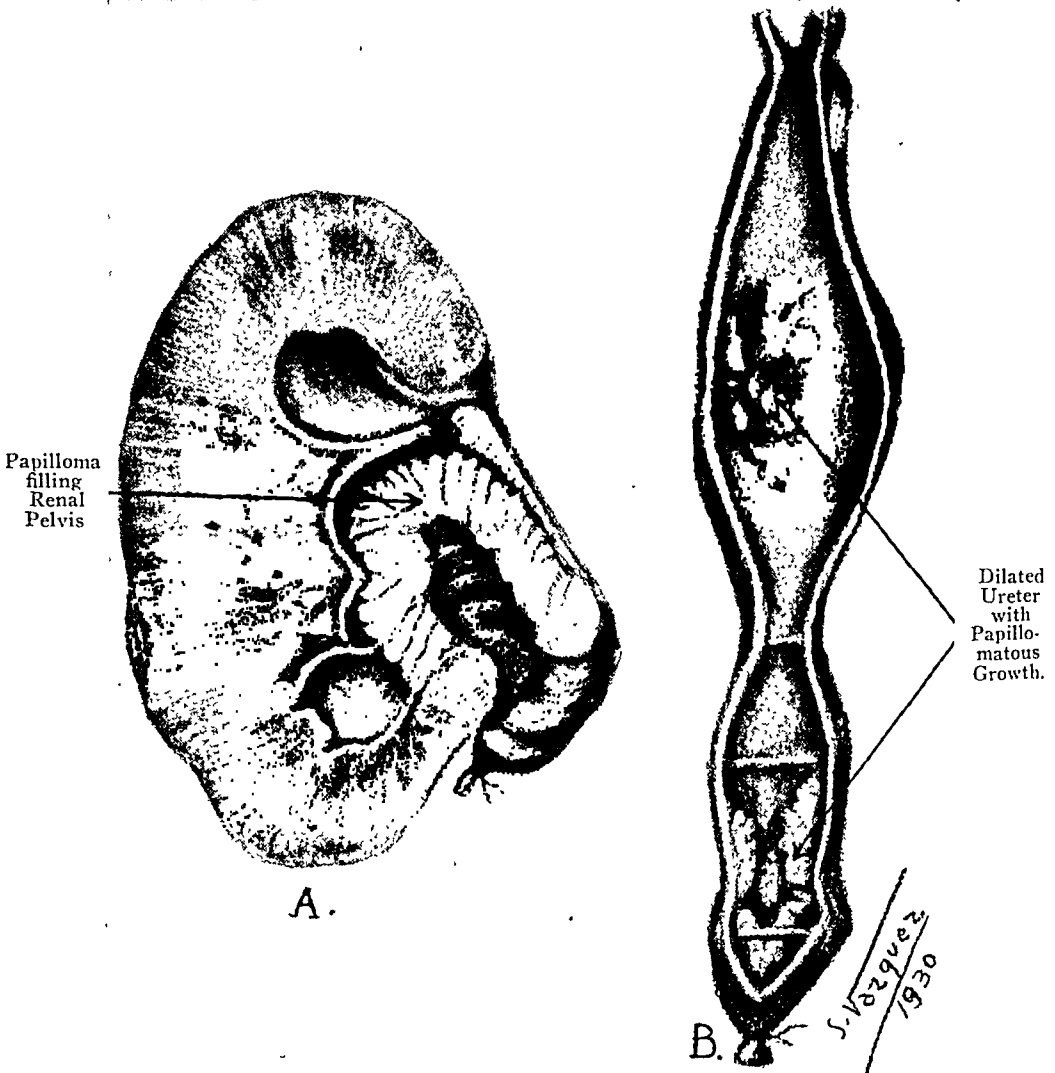


FIG. 14.—Recurrence of papillomatous growth in the stump of the ureter: a.—Patient is a doctor in whom, during an attack of painless hematuria, the pyelogram revealed a filling defect at the pelvis of the kidney, for which nephrectomy was done. b.—Two years and three months later the patient had a similar attack of hematuria, and the ureterogram revealed a filling defect for which a secondary ureterectomy was done. This case illustrates the value of the combined primary ureteronephrectomy (Walker's case).

administration of a whiff of gas and ether may be necessary. As a rule, if both procedures are carried through in one sitting, the local anæsthesia is sometimes sufficient and gives better results. The relaxation is perfect, there are no ill effects afterwards, and the recovery is prompt and uneventful.

*Surgical technic.*—As I am reporting two illustrative cases (first, one of combined aseptic ureteronephrectomy, and second, one of nephrectomy with

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subsequent ureterectomy), I feel that the operative technic will be better described separately with the description of each case.

So in this chapter I shall merely discuss the most important views of the surgical problem.

I do recommend that when the diagnosis of the pathological ureter is



FIG. 15.—Pyeloureterogram showing an enormous hydroureter and hydronephrosis due to a stenosis or congenital stricture of the intravesical ureter which obviously necessitates ureteronephrectomy.

well established the two-stage operation should always begin below by cutting across the ureter as close to the walls of the bladder as possible between two clamps and making a double ligature of both ends of the cut ureter as the first stage of the procedure for the combined and simultaneous ureteronephrectomy.

The incision to expose the pelvic ureter must be adequate to permit the free dissection of the vesical portion of the ureter and as the operation is

wholly extra- and retroperitoneal, the oblique incision parallel to Poupart's ligament, and running from about the level of the anterior superior spine downward to the semilunar line, five to six centimetres in length, is satisfactory and sufficient for a good exposure. With this semi-oblique incision no nerves of the abdominal wall are sacrificed. Neither the deep epigastric

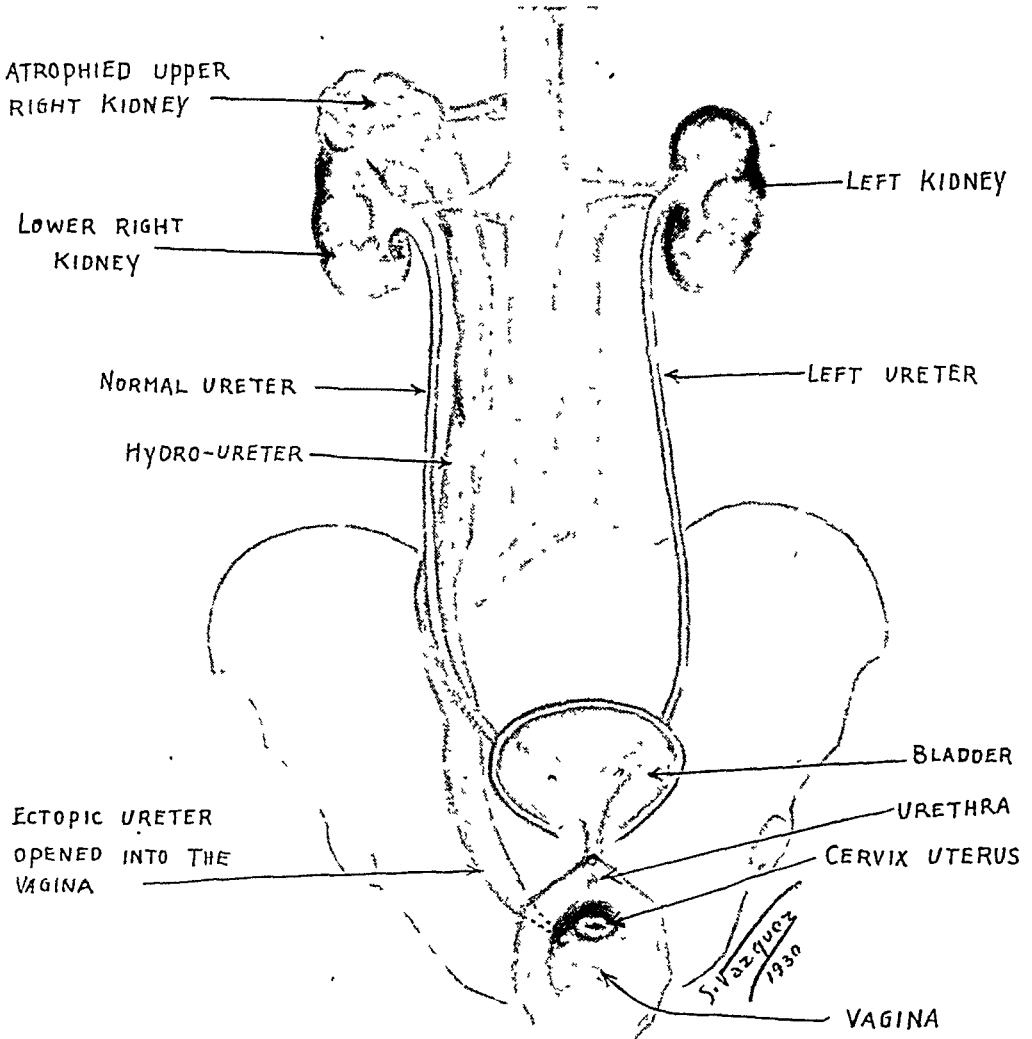


FIG. 16.—This drawing shows the congenital extravesical opening of a ureter requiring ureteronephrectomy to obtain permanent cure. The drawing illustrates the incident of a double kidney with a double ureter in which the ureter of the upper kidney opens into the wall of the vagina, associated with chronic infection, hydronephrosis and hydroureter, and a uropurulent vaginal discharge observed from birth. The other ureter of the same kidney opens normally into the bladder. This case indicates the convenience of the two-stage ureteronephrectomy or ureteroheminephrectomy (as in cases reported by Albarran, Judd, Papin, Kidd and others).

artery nor the branches of the ilioinguinal or iliohypogastric nerves are divided, so there is no danger in the future of the formation of a hernia.

The other incision that may be used in this connection is the one commonly employed in appendectomy, the transverse incision described some thirty-five years ago by McBurney, and since modified by Wier, Elliot and Dever. It is classically known as the so-called muscle-splitting operation, where the skin and the external oblique with its aponeurosis are only divided

and the internal oblique and transverse muscle are split by the handle of the scalpel. But undoubtedly where the field is restricted it offers an insufficient exposure. In dealing with a much-diseased organ and surgical ureter *per se* the urological surgeon must have sufficient space for dissection and complete exposure of the pelvic ureter, way down to the bladder wall, since sometimes a partial cystectomy for a malignant growth of the ureter and bladder may be required. There must be room to separate the entire ureter from its attachments to the parietal peritoneum by blunt dissection and to facilitate its complete removal from the lumbar secondary incision of exposure.

There is also the vertical medium-line incision at the external border of the rectus muscle, used by a few authors, but the oblique incision as here described is more convenient and is the one that affords the best exposure and gives the greatest certainty of the extraperitoneal procedure and assures an aseptic operation with no contamination of the muscles or the abdominal wall of the anterior wound, so that the incision almost always heals entirely by primary union.

In urinary surgery all the operations performed upon the kidney, ureter and bladder are, as a rule, extraperitoneal with very few exceptions, such as those for tumors of the kidney and ectopic pelvic kidney. For this last variety, when hydronephrotic infection with stone is present, the long mid-line incision is required as in laparotomy for opening the peritoneal cavity to accomplish ureteronephrectomy transperitoneally whenever possible, as Kidd has recently shown when reporting a successful case before the Royal Society of Medicine.

In ordinary cases, the second stage of this combined procedure, namely, the lumbar incision, slightly more oblique from behind or from outside-inward, is none other than the classic one of an ordinary nephrectomy: The same technic should therefore be applied, but the surgeon must bear in mind that the whole specimen should be removed *in toto*, and in one piece as soon as the ureter is isolated and pulled out; the ureteronephrectomy is an easy job. It is always convenient to drain those cases of ureteronephrectomy by leaving a cigarette drain at one end of each of the angles of the wound. For example, one may be placed below, right behind the walls of the bladder, for the purpose of securing any drainage or leakage of urine that may escape, should the double-tied ligature slip from the remaining vesical portion of the ureter or the bladder itself, while the other cigarette drain is placed in the upper angle of the nephrectomized wound close to the ligated pedicle, so as to secure drainage in case of accident. These two drains can be removed as may be convenient on the second or third day after the operation. The untouched part of the abdominal muscles which are not divided will act as a protective bridge between the two separate incisions in the event of a future eventration or hernia of the abdominal contents, particularly in the female. Another advantage is that it will divide and diminish the operative shock, which is much more desirable for the benefit of the patient. There-

fore, these two separate incisions should be preferred to the long, single, mutilating incision used in the past.

## REPORT OF CASES

CASE I.—*Nephrectomy for functionless hollow kidney secondary to multiple stone long impacted in the pelvic ureter, necessitating, four and one-half months later, a subsequent ureterectomy in order to obtain cure of an abdominal-lumbar fistula, due to the infected ureter stump that contained a small calculus.*—Patient is an Armenian, well developed and well nourished and apparently in good health. History No. 155410. Mrs. B. D., thirty-four years old, came to the Urological Clinic of the New York Hospital referred by the Gynecological Department of the same hospital on June 6, 1928, complaining of pain in left lumbar region radiating towards the lower abdomen for over three years with slight dysuria and frequent urination.

Family history is irrelevant except that father died at forty-five years of age of pneumonia and mother at thirty of typhoid fever. Patient is married, husband living, two brothers also living and well. In the past personal history, patient had the common childhood diseases without incidents. Had an attack of pneumonia in 1916 and an abdominal operation in 1925 for appendectomy. The menstrual periods began at the age of thirteen, and were always regular until the last four years, when intervals have been every two or three weeks. Has no children and there is no history of miscarriages or abortions.

Present illness started about two and one-half years ago when she began to have pain in the left back, and occasional burning when urinating. This pain has persisted except when she is lying down. It begins soon after she moves around. She has also had for the past six months intermittent pain in both lumbar regions. No history of the patient as to actual hæmaturia or pyuria, but urine analysis shows microscopic pyuria and hæmaturia. Patient was cystoscoped on June 7, 1928, but in view of the marked cystitis the exploration was discontinued and patient was advised to return twice a week for bladder lavage until the much-infected and inflamed bladder cleared up to permit complete examination. Cultures of the bladder urine were negative. The patient was cystoscoped again on June 21 and July 2, when the right ureter was catheterized, and normal specimens from the right kidney were obtained. On the left ureter the catheter met obstruction about three and one-half centimetres from the mouth of the ureteral orifice and no specimens were collected. On July 26 patient was cystoscoped again and another functional test was carried out, and also plain X-ray pictures, left pyelogram and ureterogram taken. On August 13, in another examination, I made the same observation of marked œdema of the left ureteral orifice, and that the ureteric catheter on the left side met obstruction about three and one-half centimetres from the bladder. The specimen was collected at the same time and sent to the laboratory for examination, which was as follows:

*Report of Ureteral Specimen*

|                | <i>Right</i>        | <i>Left</i>      |
|----------------|---------------------|------------------|
| Character..... | Clear               | Hazy             |
| Urea.....      | 4.5 grams per liter | 1 gram per liter |

*Phenolsulphonephthalein*

|           |            |         |
|-----------|------------|---------|
| Appeared  | 3½ minutes | No time |
| Per cent. | 0.25       | 0       |
| Time      | 10 minutes | No time |

*Microscopic Examination of Sediment*

|              |                                  |                              |
|--------------|----------------------------------|------------------------------|
| Wet specimen | epithelium, one high power field | Pus 100 per high power field |
|--------------|----------------------------------|------------------------------|

*Cultures of Urine Show:*

Right and left ureter and bladder negative.

The X-ray report was also of interest because it revealed multiple shadows along the line of the left ureter indicative of stone long impacted in the wall of the ureter. (Fig. 1.) There were no other shadows indicative of stone in the urinary tract. The left pyelogram shows (Fig. 2) a peculiar pelvis without calices and the ureterogram reveals dilatation of the ureter with filling defects here and there corresponding to the shadows seen in the plain pictures. The impression was that of a functionless left kidney with multiple stone long impacted in the ureter, and in view of the fact that the patient had perfectly good function in the right kidney, I advised her to enter the hospital and submit to an operation for nephro-ureterectomy in order to remove the functionless kidney together with the ureter and the multiple calculi long impacted in the same left ureter. Patient was admitted to the hospital two weeks later on August 27, and on the following day I performed under paravertebral anaesthesia a left nephrectomy with the usual technic. The much-diseased ureter containing the incrustrated calculi was removed as low down as possible through the limits of the lumbar incision, and, because the patient's general condition was not very good for prolonging the operation, the incision was extended down for the complete removal of the ureter. Then a ligature was placed as low down as possible and the ureter cut across in the usual manner. Hence a ureter stump about four centimetres in length was left behind, with two cigarette drains in each angle of the wound—one around the stump of the ureter and the other in the renal fossa. The wound was then closed in layers, using catgut for the deeper structures, and the skin closed in the usual way with interrupted sutures of silkworm gut.

The small atrophic kidney, together with the long dilated ureter containing the calculi, was sent to the laboratory for examination, but, unfortunately, the whole specimen was carelessly lost. This is why I am sorry that I cannot present it on this occasion. The calculi were composed of calcium and earthy phosphates. Patient's convalescence was totally uneventful. She was up on the eleventh day and discharged from the hospital on the sixteenth day after operation, with the wound closed and in good condition.

However, about a month after the operation, she returned to the clinic complaining of pain in the lower abdomen with pyuria and frequency of urination. The nephrectomy wound had healed, but there was a small sinus at the lower angle of the line of the incision discharging a little pus and urine. Otherwise the general condition of the patient was excellent. On cystoscopy the bladder was negative, except for flakes of pus at the fundus and slight congestion throughout the bladder mucosa. The right ureter was catheterized and a clear specimen obtained. In the left ureter, from which the left kidney had been removed, the ureteric catheter entered the ureter for only about one and one-half centimetres from the mouth of the ureteral opening. The right kidney and the stump of the left ureter were irrigated with a solution of revonol dextrose 1 to 2000 with the result that the color dye injected in the stump of the left ureter came through the abdominal-lumbar sinus. The patient was treated cystoscopically on several occasions by irrigations of the stump of the ureter, dilatations with bougies, manipulations with the corkscrew ureteric bougie, and fulguration of the intramural ureteral orifice, with the hope of removing an incrustrated stone lying in the pelvic ureter; but the stone did not pass and the fistula and other urinary symptoms persisted. In order to corroborate the clinical findings, plain X-ray pictures and ureterograms of the ureter stump were taken, which revealed the presence of the incrustrated calculus in the lower ureter; and the injection of sodium iodide showed a persistent fistula from the ureter to the skin. (Fig. 3.)

As the patient did not improve and the lumbo-abdominal fistula continued to discharge pus and urine, besides being painful and troublesome, she was admitted to the hospital again on January 8, 1929, for a secondary ureterectomy done with a view to



removing the calculus and the infected ureter stump in order to relieve the symptoms and cure the complication of the uropurulent abdomino-lumbar fistula.

*Operation for secondary ureterectomy.*—Ether anæsthesia was administered in the usual manner, the patient having been previously cystoscoped and a No. 6 ureteric catheter left *in situ* in the stump of the left ureter.

A left inguinal incision was made about four inches long through skin and fascia. Muscles and other tissues in this region were separated by blunt dissection until the wall of the bladder was exposed. In the course of this dissection a small opening was made into the peritoneum, which was sutured up immediately. During the attempt to dissect the fistulous opening the peritoneum was again opened and was again sutured together before proceeding with the rest of the operation. After the bladder wall had been exposed it was possible to locate the stump of the ureter, which contained the small stone diagnosed at a previous cystoscopic examination. The ureteral catheter which had previously been placed in the stump was finally located, but dissection of the surrounding tissue was rather difficult on account of its location. Finally, however, the ureteral stump itself was located and freed from its surrounding tissues, and the bladder wall opened. The finger was now inserted into the bladder and the ureteral orifice located, which made the dissection easier. The stump of the ureter was grasped by a pair of Allis forceps and a small incision made, removing the stone with a piece of the ureter. Two stones were readily found, which were slightly adherent. They were removed with a piece of the stump of the ureter; the stump wound was cauterized with carbolic and alcohol and left without suturing. A counter incision was made about ten centimetres to the left of the mid-line and about midway between symphysis and umbilicus.

A suprapubic catheter was placed for the purpose of drainage since the bladder had been opened. Several cigarette drains were placed in the left lower quadrant, for the purpose of draining this area.

The incision was closed in layers using plain catgut for the muscle and fascia and silkworm gut for the skin.

Patient returned to room in good condition. She had rather a slow convalescence and the wound drained profusely through the cigarette drain, but no urine came through, due to the fact that the suprapubic tube drained very well. On the ninth day after operation the suprapubic tube was removed and a catheter was put in the urethra to secure drainage and promote the healing of the wound. On the thirteenth day, temperature was normal and the wound was still discharging pus. However, the patient's general condition was excellent. The indwelling urethral catheter was removed on the twenty-third day after operation and four days later the wound appeared to be almost healed, and the patient, having normal temperature and feeling well, was discharged as cured.

She has been coming down to the clinic for bladder lavage, but the wound is firmly healed, her general condition is good and the bladder cystoscopically appears to be normal.

*Résumé.*—This patient had a long history of suffering and discomfort due to the pathological condition of the ureter resulting in kidney atrophy. While she responded very well to the operations that were performed on different occasions, in order to bring about permanent cure, the incidents of this case illustrate well how much more advantageous it would have been for the patient and how much easier for the surgeon if the diseased kidney and the ureter in its entire length had been removed all in one sitting, thereby sparing the patient the common complications observed from the infected ureter stump.

## COMBINED URETERONEPHRECTOMY

CASE II.—*Combined ureteronephrectomy for tuberculous, functionless kidney with megalo-ureter, carried out for the total removal of both the diseased ureter and kidney in two stages and in one sitting.*—Miss B. L., a thin, rather feeble-looking young girl, seventeen years old, on September 25, 1929, came to the Urological Department of the New York Hospital accompanied by a social service worker who stated that the patient had been suffering with pus in the urine and frequency of urination for the last ten



FIG. 17



FIG. 18

FIG. 17.—Case II, Ureteropyelogram revealing the presence of megalo-ureter or hydropyoureteronephrosis without function. Author's case as herein reported, illustrating the indications for a combined primary ureteronephrectomy.

FIG. 18.—Ureteropyelogram of the kidney and entire ureter both successfully removed in one piece and without opening by combined ureteronephrectomy (Author's case).

months and that she had been examined and cystoscoped elsewhere but no definite diagnosis or explanations of her symptoms had been made.

*Family History.*—Patient is single, father and mother living and well, has two brothers and two sisters, all living and well also, and there is no history of tuberculosis in the family.

Past personal history is of interest in that the patient had been treated for cardiac disease for over eight years and that three years ago she was in a hospital for a nervous breakdown condition and rheumatism.

A year ago patient had an attack of cystitis with fever and frequency of urination and was confined to bed for two weeks, at which time she was treated with urinary antiseptics. At present she says she can walk moderately fast on a level without embarrassment, but she cannot run or go up steps without becoming short of breath. There is no cough or hæmoptysis. Tonsils had been removed. She had also suffered at times in the past, with dysmenorrhœa and amenorrhœa. With ovarian extract medication she had come back to her normal menses.

After I took the above history on the day of her arrival at the hospital, I cystoscoped the patient and was able to find the interior of the bladder chronically inflamed, with a considerable amount of flakes of pus lying at the fundus and much redness and congestion throughout. The ureteral orifice on the left side was markedly œdematous and swollen, giving the impression of a certain degree of ureterocele or that of an impacted stone in the intramural portion of the ureter. Both ureters were catheterized, a specimen from each side and also one from the bladder were sent to the laboratory for cultures, urea and microscopic examination, and patient was advised to return in a week's time to prepare for the urographic examination.

One week later, September 30, cystoscopy confirmed the previous finding, with definite impression of good phenolsulphonephthalein output from the right kidney, while there was practically no function on the left side. Plain X-ray pictures and left pyelogram were taken, injecting about fifty-five cubic centimetres of sodium iodide 20 per cent. with patient in the erect posture for the ureterogram. The X-ray report shows no shadows indicative of stone in the urinary tract, but the left ureteropyelogram (Fig. 17) reveals a much-destroyed kidney pelvis with a tremendous megalo-ureter or hydro-uretero-pyonephrosis, giving the impression of tuberculosis of left kidney and entire length of ureter, for which operation patient was advised to enter the hospital.

*Operation.*—October 11, 1929, using paravertebral anæsthesia and block infiltration with procain 1 per cent., and having previously cystoscoped the patient for the purpose of leaving the indwelling ureteric catheter fixed in the left ureter, with the patient in a slight Trendelenberg position, a left abdominal oblique incision was made about five centimetres long at the outer border of the left oblique abdominalis muscle, and running from McBurney's point obliquely inward and downward to a point about the semi-lunar line. The incision was carried through the muscle and outer border of the peritoneum, this serosa being separated bluntly to find the ureter adherent and behind it. The much-dilated ureter containing the indwelling catheter was then isolated from the peritoneum and other structures of the lower pelvis. The round ligament and the uterine artery were dissected away, and neither structure divided. The ureter was exposed down to the bladder and ureteric inlying catheter pulled out from below by an assistant; then the ureter was divided between two clamps placing a double ligature on each end of the ureter. Both proximal ends of the ureter were cauterized with carbolic and alcohol and the upper free ureter was covered with several pieces of gauze and dissected upward as high as possible so that it could be reached entirely from above during the second stage of the operation or through the lumbar incision for the total removal of the kidney and ureter. The divided free ureter was then replaced in the wound and the incision closed by layers in the usual manner, leaving a cigarette drain placed down in the lower angle and directly behind the bladder. (Fig. 19.)

For the second stage of the operation the patient was turned over on her right side, fixed for kidney position. A left lumbar incision about seven centimetres long was made running from the costovertebral angle at Henle's ligament obliquely downward and outward about three or four fingerbreadths above and away from the upper edge of the iliac crest and the part where the first abdominal incision was made, so as to leave a

## COMBINED URETERONEPHRECTOMY

bridge of abdominal tissue and muscles undivided, separating the two incisions, this being done to preserve a point of resistance in the abdominal wall.

After incision of the superficial tissues and the plane of muscles of that region, the transversalis fascia was divided and then the perirenal fatty capsule incised from behind and split lengthwise by the fingers. The kidney was found small and adherent, and the diseased ureter, already free from its attachments, was readily identified and delivered after further blunt dissection. (Fig. 20.)

To free the upper and lower poles of the kidney the pedicle was clamped and a double ligature made, removing the kidney and ureter all in one piece and without opening. All bleeding points were tied and the wound thus dry, was closed in the usual manner by layers, leaving a cigarette drain down in the renal fossa and at the upper angle of the lumbar incision. Patient returned to the ward in good condition and after an uneventful recovery in twenty-seven days left the hospital in good condition.

The post-operative care was satisfactory, the cigarette drain was removed on the fourth day and the stitches on the sixth day. The first abdominal incision healed by primary union without incidents while the renal wound discharged pus for several days, delaying the complete healing of the lumbar wound. However, the patient left the hospital with the wound closed and in excellent condition, and went to the country for convalescence.

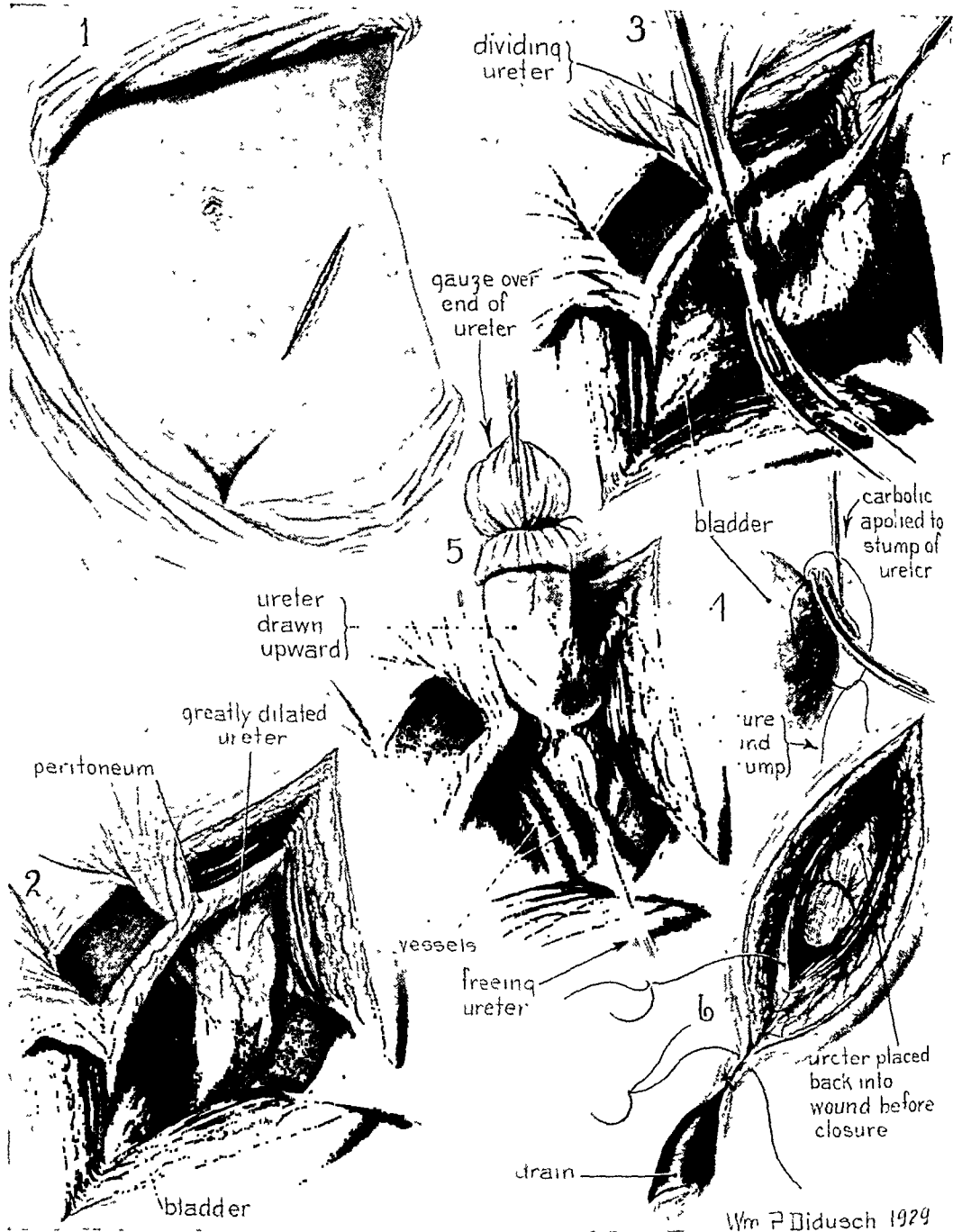
I cystoscoped this patient two months after she left the hospital and found her bladder free from symptoms. Recently (about seven months after the operation) I have seen her again. She is enjoying good health, has gained thirty-four pounds, and is free from urinary disturbances.

*Résumé.*—This case illustrates the value of a combined ureteronephrectomy and the convenience of employing this method of a two-stage operation in one sitting, which is suitable for cases of this type, and which, although it appears to be radical, is in reality a conservative procedure and is a means of obtaining permanent cure without complications or the common troubles caused by the infected ureter stump.

### SUMMARY

In summarizing this study in a practical way, as the writer proposes to do, attention must be drawn to the most important clinical and surgical features of this operative procedure as a means of permanent cure at a single sitting, saving the patient from prolonged suffering, and shortening the time of convalescence. Among the many advantages of the two-stage ureteronephrectomy are: first, it divides the operative shock by the two separate incisions; second, it preserves the resistance of the abdominal wall against herniation; and third, by cutting across the ureter behind the bladder in the lower abdomen, in the first stage of the operation, it makes the surgical procedure one of very simple technic and one that is anatomically avascular, a very important consideration, since, this being an aseptic operation, the wound heals by primary union.

There is no handicap of contamination of the walls of the wound carried downward from the already infected kidney because, being in two separate and distinct fields, the procedure affords less chance of reinfection or of any damage being done to the peritoneum in opening it. The operation is quickly accomplished and the patient does not experience any greater



Wm P Bidusch 1929

FIG. 19.—Operative technic—first stage. (1) With the patient slightly in the Trendelenberg position, an incision is made running from McBurney's point obliquely down to the semilunar line, cutting the skin and superficial aponeurosis of the external oblique and internal oblique muscles, in the direction of the incision. The peritoneum is then exposed and gently retracted by blunt dissection, thus separating it from its pelvic attachments. (2) The ureter containing the indwelling catheter is now readily identified and is always found closely adherent to the retracted portion of peritoneum. By still further blunt dissection the ureter is easily isolated down to its junction with the bladder practically without cutting any blood vessels. (3) The indwelling ureteric catheter is pulled out from below by an assistant and the diseased ureter greatly dilated is retracted and readily exposed down to the point where it reaches the bladder wall; two clamps are then fixed in position and the ureter divided, the field being covered with gauze to avoid any possible drop of urine or contamination. (4) The divided ureter is cauterized with carbolic and alcohol and a double ligature of the stump of the ureter made very close to the bladder wall, letting the bladder drop back into the pelvis. (5) The other end of the divided ureter is also ligated and a piece of gauze wet in alcohol tied around it to prevent any leakage of the ureter contents that might lead to contamination of the wound. The ureter is then dissected upward and separated from its attachments to the peritoneum and other structure, so that it will be entirely loose and ready for its removal from above during the second stage of the operation. The anatomical exposure is very satisfactory; the widely dilated ureter is easily freed and practically no bleeding is encountered. (6) The ureter is then placed back within the wound before closing, leaving a small cigarette drain at the lower angle and just behind the bladder for the purpose of securing drainage if any leakage of urine should occur. The wound is closed in layers in the usual manner. A dressing is applied and the patient is turned over and prepared immediately for the second stage of the combined uretero-nephrectomy.

reaction than in an ordinary nephrectomy. Finally, the surgeon feels sure that he has accomplished his duty and that obviously the patient will not have reflux, lumbar fistula, pyuria, hæmaturia, colic pain, bladder discomfort or any other complications or sequels from the infected ureter stump which, in many instances, are revealed later. We must also not forget that the science of surgery is a specialized art. It is therefore essential that we should try to preserve the body's lines in an artistic manner. Thus the two separate incisions both afford safety and also give sufficient room for a perfect anatomical exposure. By not cutting entirely across the belly walls with the long single lumbo-ilioinguinal incision, we achieve the result that the undivided muscles, nerves and blood-supply will not only keep the body's lines in a more artistic and efficient manner, as is desired, but will also serve for the preservation of better function in years to come.

My first case report shows how difficult for the surgeon, and particularly for the patient, after a long period of suffering, is a secondary operation for ureterectomy when the ureter is chronically inflamed and densely adherent to the peritoneum, bent down, or plastered to the lower pelvic structures. It further calls attention to the troublesome sinus infection and scar-tissue formation from the previous operation which sometimes limit the operative field and make impossible any ligature in the low ureter. It emphasizes the continuous fear of working under difficulties and the risk of damaging the bladder or peritoneum or even the iliac vessels—complications which the surgeon must try to avoid. As the patient is put in the exaggerated Trendelenburg position during the first stage of the ureteronephrectomy, the peritoneum is loosened and easily retracted and protected with gauze, so that the abdominal contents are readily pushed back, giving a clear anatomical exposure which makes the whole procedure easier and more feasible. The report of my second case illustrates the practical surgical conception of this combined method of ureteronephrectomy in which the diseased ureter, clearly recognized before the operation, and the pathological kidney, all "en masse," could be removed in one sitting, in one piece and without opening, thus conforming with the paramount desideratum of carrying out an aseptic operation. During the first stage (Fig. 19) of this combined ureteronephrectomy, as I illustrated in the report of my second case, the ureter, which is always adherent to the parietal peritoneum, is readily identified by the palpation of the indwelling ureteric catheter previously placed in position by cystoscopy, which facilitates and shortens the procedure even in the most difficult cases to be encountered.

A survey of the literature, as well as the clinical experience of other authors, leads to the conclusion that probably an increasing number of these complications observed after nephrectomy could successfully be prevented by the use of this combined surgical method. If certain principles of surgical interference could be recognized, this method which, although radical in principle, is conservative in essence, could without any doubt in my mind be employed more widely with full confidence in the safety and convenience

plishing immediately afterward the second stage of the combined uretero-nephrectomy by the usual lumbar incision of an ordinary nephrectomy. (Fig. 20.) This I have tried to illustrate with the report of my second case, where the final results obtained were satisfactory and most gratifying.

## CONCLUSIONS

1. Combined ureteronephrectomy in one sitting and in two stages is a practical and feasible operation that should be performed whenever the ureter is diseased or involved in the pathological condition of the kidney.

2. The pre-operative diagnosis and recognition of the clinical entity is most essential, and for this cystograms, ureterograms, pyelo-ureterograms and pyelograms are indispensable. Moreover, when catheterization of the ureters is impossible, intravenous urography is decidedly helpful.

3. The most common indications for ureteronephrectomy are described in Table I, and the sequels or complications caused by an infected ureteral stump left behind at the time of nephrectomy, which requires a secondary ureterectomy, are summarized in Table II.

4. The operative technic of ureteronephrectomy *versus* nephro-ureterectomy is herewith described, and the convenience and advantages of the two-stage operation are discussed.

5. Many of the common complications of the nephrectomized wound, particularly in renal tuberculosis, are due to secondary infection, bacillosis of the muscular walls, trauma during the surgical procedure from lack of exposure, secondary abscess formation in the renal fatty capsule, and the infected ureteric stump left behind at the time of nephrectomy.

6. In about 18 per cent. of all surgical conditions of the kidney the ureter is involved and its total removal is indicated. Therefore, whenever the ureter is diseased its entire length should be removed *in toto* by uretero-nephrectomy or by ureterectomy subsequent to nephrectomy.

7. The cause of the delay in healing of a nephrectomized lumbar wound, in addition to infection and contamination, is in many instances an infected stump ureter; also the phenomenon of an uropurulent lumbar fistula or urinary reflux after nephrectomy, on that side, is due mainly to a patent ureter or tuberculous ureteritis of the ureteric stump.

8. When the diagnosis is perfectly established and the surgeon plans to remove kidney and ureter in one piece without opening it, the first step of an aseptic ureteronephrectomy should start from below, cutting the ureter behind the bladder, in such a way that the second stage through the lumbar incision may serve to accomplish the complete removal.

9. In tuberculosis of the kidney, as well as in any other pathological condition that necessitates its removal, if the ureter is not involved or diseased, nephrectomy alone will bring about permanent cure.

10. The useless stump of the ureter left behind after nephrectomy, if not diseased or involved in a true pathological process, gradually becomes atrophic, its lumen obliterated, and the whole is seen as a fibrous, function-

less cord in from nine months to three years as clinical observation and animal experimentation have demonstrated.

11. It is obvious that the best indication for a combined ureteronephrectomy is, in addition to a clear-cut diagnosis, the assurance of a sound kidney with good function on the opposite side.

12. This surgical procedure of combined ureteronephrectomy is sound and conservative, has definite indications and affords permanent cure.

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## EXTRAVASATION FROM THE URETER

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EXTRAVASATION at any level of the urinary channel commonly precipitates a surgical problem of immediate and grave significance.

The condition is usually the result of some external traumatism and most frequently involves the lower tract, though no segment of it is immune. The septic and gangrenous individual whose urethra has been torn in an accident or punctured by violent instrumentation is the occasional dreaded visitant of every urologist. Crushing injuries to the pelvic girdle not infrequently result in damage to the bladder with an escape of its contents into the tissues. The renal pelvis may share the injury which fractures a kidney or may be torn from its attachment to that organ; a hydronephrotic pelvis may be ruptured when suddenly subjected to great compression. The size, structure, and location of the ureter make it the least vulnerable zone in the urinary system, but extravasation may result here also from bullet or stab wounds, from damage in the course of operations upon adjacent structures, and from overzealous manipulations with ureteral bougies, dilators, and metal stone-extractors.

The extravasation which occurs in the absence of any of these external forces is much more unusual. Perhaps the most common illustration of this type is the sweeping infection which sometimes results when periurethritis has caused a mucosal break sufficient to allow just enough urine to get through to inoculate the tissues with streptococcic or anaërobic organisms of intense virulence. More rarely, so-called spontaneous rupture of the bladder is encountered, usually as the result of the efforts of its own musculature to overcome some obstruction, such as an hypertrophied prostate; a case of this sort with the discharge of the entire bladder contents into the peritoneal cavity was reported by the writer some years ago. Most rarely of all the ureteral or pelvic wall may yield to some force acting from within, and it is this particular aspect of the lesion of extravasation which will be discussed in connection with the description of three cases.

*Etiology.*—A rather hurried consultation of the literature has been almost barren of results. Data doubtless exist dealing with reports of similar cases but it has not been easily available. Young discusses ureteral trauma at some length, but only with reference to external violence; and the same is true of a recent article by Legueu. Lower and Belcher refer very briefly to the well-known but rarely encountered possibility of tubercular ulceration through a ureter with fistula formation. In an admirable review of the surgical importance of the ureter Kirwin has no mention of the condition under consideration here. Wallenstein discusses urinary extravasation at

varying levels, reports a series of cases, and includes one of great interest involving the renal pelvis. Twenty-five years ago, Henry Morris referred in so many words to ulceration from calculous or tuberculous ureteritis as one of the causes of ureteral fistula. With his customary insight and vividness of expression Keyes goes clearly to the point. Declaring that the pathology of calculus in the urinary tract consists of retention, ulceration, and infection he says:

"Ulceration occurs at whatever point in the calyx, the pelvis, or the ureter a stone may rest. If the stone is small and movable the ulceration may be insignificant. If it is large or impacted the ulceration may be so deep that actual perforation occurs, permitting the stone to escape from the kidney, the pelvis, or the ureter into the surrounding tissues. This complication, associated as it is with urinary extravasation, is as unusual as it is grave." And again when enumerating the possible effects of a stone within the ureter: "The ureter ruptures by (a) acute gangrene or (b) ulceration about an encysted stone. The result is usually acute retroperitoneal phlegmon, infiltration of urine, abscess, fistula. Rarely an encysted stone escapes silently into the retroperitoneal tissue."

This quotation from Keyes seems to describe accurately the etiologic ground work of all our cases and will be adopted as the basis for discussion without any further consideration of other possible but very remote causes of ureteral extravasation arising from within.

*Symptoms and Diagnosis.*—The clinical picture will usually, at the moment, be dominated by the evidence of sepsis of some degree due to the infection that almost inevitably attends urinary extravasation. If the condition is progressive and active the patient will be desperately ill and urgently in need of intervention. If, on the other hand, local tissue reaction has effected a walking-in of the process the situation will be less dramatic and will in many respects simulate the perinephritic abscess better known in association with other causes. Actually, as Keyes indicates, an encysted stone may escape "silently" into the tissues and produce no local or general disturbance of any moment, but this must be quite rarely true.

The antecedent history will be of great significance and, as might be presumed, will be concerned especially with one or more attacks of severe renal pain (or colic) due to the presence of calculus in the ureter. Vesical disturbance may or may not be present, and the urinary microscopic findings, if any analysis has been made in this stage, may be indicative of trouble in this area.

When a septic patient with this previous history of renal colic presents himself and physical examination discloses muscular rigidity and marked tenderness in the renal area anteriorly and posteriorly—or a palpable mass—ureteral extravasation may be suspected but probably will not be, owing to the rarity of the condition and the uncertainty of such a diagnosis. Even when a preliminary X-ray plate defines a suspicious shadow in the neighborhood it is more likely that the condition will be considered due—as is

generally the case—either to acute diffuse renal infection or to ureteral block with acute retention in the pelvis. The urologist will therefore be disposed to make prompt cystoscopic exploration with the hope of relieving such a block, if present, and preventing disaster to the kidney, pending such subsequent attention to the calculus itself as circumstances may dictate. If it be found impossible to reach the kidney with a catheter the further course of the case will probably lead to exploratory operation and the drainage of a supposed perinephritic abscess, the true condition coming to light later if at all. If, however, the catheter can be advanced to the pelvis or the zone of extravasation purulent urine or actual pus will be evacuated and the urologist will probably content himself with this for the time being, awaiting the subsidence of fever and sepsis before proceeding by means of pyelography to obtain a better definition of the local situation. During this interval the diagnosis will remain undisclosed since it is dependent entirely upon pyelography. The latter may be hastened by failure of the patient to improve under catheter drainage; or the urologist, for reasons that appear sufficient to him, may deliberately undertake primary pyelography at the outset, which usually is undesirable, sometimes dangerous, in the presence of acute renal infection, but which under certain unusual circumstances may be much less undesirable and dangerous than either delay or blind exploration. It may be objected that with ureteral extravasation—if one could anticipate its existence—pyelography is never justifiable, but with this viewpoint the writer is not in agreement. The distribution of a small amount of sodium-mercuric iodide into tissues already infiltrated with pus and urine is not likely to be productive of any serious sequelæ, if very low (gravity) pressure is used, which is our invariable custom; and the information furnished by the extension of even a trace of this solution beyond the confines of the ureter is of paramount importance.

In our cases the clinical details were essentially in accord with the above generalizations. Pain was conspicuous in the previous history of all three. In one the overwhelming fact of total anuria obscured everything else, though it is to be noted that the patient had fever and a very high blood count. In the other two sepsis was obvious; one of these presented striking local findings, the other did not. Shadows were present in the X-ray plates of all three. In one the diagnosis was disclosed (unexpectedly) at autopsy; in the other two it was established by pyelography.

*Prognosis and Treatment.*—The condition is admittedly grave. When the actual leakage of urine is minimal in amount and the tissue reactions are prompt and efficient localization of the process may be accomplished, with or without the development of a circumscribed abscess; under these circumstances the patient may actually recover without any surgery whatsoever, as happened in one of our cases. On the other hand, leakage may be more extensive or more continuous, tissue reactions may be less effective, organisms may be more virulent; devastating phlegmonous or gangrenous infection

or septicæmia may then ensue, and the patient may quickly develop a clinical problem of extreme danger and difficulty.

In view of this latter eventuality it must be accepted as a working principle that extravasation of urine, wherever located and from whatever cause, is a frank surgical condition. The imperative immediate indication when the process is early and active is simple but efficient drainage to control infection and save life; the underlying cause of this condition can be approached later or not, according to circumstances. If the patient comes under observation later, and in the meantime has apparently effected localization of the process, surgery may be undertaken with less haste; the situation may then justify some attempt at accuracy of diagnosis and preliminary catheter drainage and other measures may improve the patient to the point where not only drainage of the area of extravasation can be established but the fundamental underlying or consequent pathology can be attacked at the same time, making secondary operation unnecessary. During this period of conservative management the patient must be kept under very close observation and prompt intervention must be substituted upon the slightest indication.

The ultimate operative procedure will depend upon a variety of possible circumstances making generalizations impracticable. Following primary drainage the situation may adjust itself; the calculus may be expelled or may remain quiescent in the tissues, the ureteral fistula may close spontaneously, and the kidney may overcome the infection and resume its function wholly or to a considerable extent. If a fistula persists, or if the continuity of the ureter has been broken, the ideal procedure would be repair but would be difficult, perhaps impossible, in the presence of the infiltration and adhesions resulting from the extravasation. Nephrectomy would then be necessary and would be required also when the kidney has become riddled with infection, as was the case in one of our patients. Finally, if the calculus remains in the ureter, or if other calculi are present in the kidney, an additional problem is introduced. Broadly speaking, therefore, the time and type of surgery will have to be determined in the light of the circumstances existing in the given instance.

#### CASE REPORTS

CASE No. I.—A. G., white, male, age sixty-seven, was sent into the hospital anuric in January 1927. For ten years prior to that time he had suffered urinary difficulty from hypertrophy of the prostate, operation for which had been discouraged by two noted urologists. At intervals he had brief spells of acute retention requiring catheterization. Such an attack had occurred about three weeks before he came under our observation. A single catheterization relieved him of this. Urinalysis and blood chemistry at that time were normal.

Five days before he entered the hospital he became quite ill, with chills, fever up to  $103^{\circ}$ , violent pain in the left renal area, which soon subsided and did not recur, some aching in the right side, and a considerable amount of blood in the urine. Three days later he was unable to void and catheterization showed the bladder to be empty. When seen by us he had been in this anuric condition forty-eight hours. General examination disclosed moderate hypertension, grossly infected and enlarged tonsils, and an enormous

prostate. The bladder contained no urine. An X-ray plate showed some suggestive but indefinite shadows in the region of the left kidney and along the course of the upper right ureter. Cystoscopy was attempted but was prevented by a massive median lobe barrier.

Heroic measures to relieve toxæmia and stimulate renal activity resulted in nothing. Bilateral nephrotomy was suggested but agreement could not be reached among consultants.

The creatinin advanced to 10.5 milligrams and the patient became comatose and died, three and a half days after he entered the hospital. Anuria persisted to the end. A partial autopsy was permitted. The X-ray shadows were now found to represent urinary calculi; other small sand-like concretions not visible in the plate were also present; both upper ureters were blocked; both pelves were dry; at the uretero-pelvic junction on the left side perforation had occurred through a partially gangrenous patch from stone pressure; from this point suppuration had begun to spread through the perirenal tissue.

CASE No. II.—R. H. B., white, male, age fifty-two, entered hospital in February 1928 with severe pain in the right renal area, radiating downward along the course of the ureter, and with a history of two similar attacks in the course of the preceding five years on the same side, and two others on the opposite side. Upon one occasion he passed a small calculus. The present spell appeared to be the worst in the series and the patient looked quite sick and somewhat septic. His temperature was 101° and his urine was loaded with pus. There had been no striking vesical disturbance, though at times the patient had experienced some difficulty getting his stream started, and his urine occasionally burned him. The remainder of the history was essentially negative with the exception of constipation, flatulence, and some shortness of breath on exertion. Physical examination disclosed only some enlargement of the heart, some disturbance of the cardiac rhythm, and some tenderness and enlargement of the right kidney. The left renal area appeared normal in an X-ray plate; indistinct calcified patches were present in the region of the bladder and of the right kidney.

Cystoscopic exploration revealed moderate gross cystitis and a veil-like floating mass in the bladder accounting for the shadow visible in the röntgenogram; the bulk of this was washed out through the cystoscope. Catheters were passed to both pelves—easily on the left—after overcoming some resistance in the lower ureter on the right. There was a normal drip from the left catheter, with negative urine and a good output of dye; on the right side the urine was under some tension, about fourteen cubic centimetres was aspirated, the specimen was full of pus and the dye output was a bare trace in nineteen minutes. All specimens were surprisingly acid in reaction. A small amount (six cubic centimetres) of iodide solution was allowed to run into the right pelvis but did not fill it though it was sufficient to identify the shadows in this area as thin calcareous material, probably identical with that observed in the bladder.

Catheter drainage of the right pelvis was maintained for two days and was productive of marked relief. Relapse promptly occurred when the catheter was removed and it had to be replaced. Temperature, blood chemistry, and blood counts responded to drainage and regressed when it was stopped. Mercurochrome intravenously, and other lesser measures, were apparently of some additional benefit. As this process could not be kept up indefinitely, however, pyelography was again attempted to determine some better cause of the behavior of the patient and perhaps point the way to some more lasting relief. A larger amount of solution was now run into the pelvis which became fully distended, exhibiting marked distortion and extravasation apparently through the ureter into the tissues opposite the third lumbar vertebra.

The necessity of operative intervention was now quite obvious but as the patient's general condition was poor and as he regularly improved when satisfactory catheter drainage was maintained this was deliberately continued as a preliminary. The right

catheter, the tip of which was lying in the top calyx, was pulled down somewhat and was retained for some days. Eventually the patient reached a point where, though definitely better, he seemed at a standstill. Operation was performed the same day, and as the kidney had shown no consistent ability to recover its function it was removed. Dense adhesions and peri-ureteral infiltration made the procedure somewhat difficult. The point from which the extravasation occurred was not clearly located. Microscopically the kidney exhibited marked chronic nephritis superimposed upon which was an acute diffuse suppurative nephritis with multiple abscess formation. The wound was troublesome for a time but eventually healed solidly and the patient to-day is in excellent condition locally and generally.

CASE No. III.—C. C. B., white, male, age thirty-seven, came under observation in December 1928 for persistent disability and continuous decline in health since a brief spell of violent sub-costal and lumbar pain on the right side two weeks previously. Beyond this incident there was no antecedent history of any consequence. Bladder disturbance was conspicuous by its absence. Severe pain was no longer present but there was a dull ache and soreness in the upper right quadrant, where there was also a palpable mass taken to be a grossly enlarged kidney. The urine, previously full of pus and blood, was now practically negative. A preliminary X-ray plate showed a small round shadow opposite the fourth lumbar vertebra on the right side, several smaller shadows in the general direction of the renal substance on the same side; and two minute questionable shadows opposite the third lumbar vertebra on the left side. The patient himself appeared washed out, anæmic and septic and he complained of having lost a great deal of weight.

Cystoscopic exploration disclosed that on the left side the urine, the pyelogram, and the function were normal. A minute shadow was identified as a calculus in the lower calyx. On the right side no urine was coming from the orifice but pressure over the kidney finally brought away a swirl of milky fluid. When a catheter was passed to the pelvic level thick pus was aspirated, followed by a thinner accumulation, and simultaneously there was definite reduction in the palpable mass in the upper abdomen. There was no dye excretion whatsoever from this side. The shadows previously noted were identified as calculi in the ureter and kidney. The pyelogram indicated considerable pathology, but most important of all there was adjacent to it the evidence of considerable extravasation, probably through the upper ureter.

Immediate operation was urged but not accepted. The patient disappeared from sight and was presumed to be dead. Six weeks later he walked into the office and announced that he was now prepared to go ahead with the operation. He was almost unrecognizable. His complexion was ruddy, he had regained a great deal of weight, he was free of pain, his right kidney was still palpable but much reduced in size and his bladder urine was now frankly purulent. A further cystoscopic review showed that the small shadow on the left side had increased markedly in size; there was now a sprinkling of pus cells in this urine, and the functional dye output was well in excess of normal; the pyelogram was essentially normal. On the right side, a calculus was encountered in the lower ureter and was passed after some difficulty; much pus again presented here, but the functional dye output, previously non-existent, was now one-fifth of normal, showing some tendency of the kidney to recover itself. The pyelogram showed startling improvement—not only in the contour of the pelvis but also in the shrinkage and sharp localization of the zone of extravasation; the general kidney outline was also much reduced in size.

A revision, if not a complete reversal, of judgment seemed to have been dictated by unexpected events during the six weeks that had elapsed. Evidently catheterization and drainage at the original exploration opened an outlet for the accumulation in the right side which was still discharging itself into the bladder, relieving the tension on the kidney and ridding the patient of his sepsis. In the meantime the speck-like shadow on



the left side, which up to now had been treated with contempt, was assuming threatening proportions. With some misgivings, but with the reassurance of the patient's progress and the fact that he was under close observation, a new program was mapped out—namely, the conservative control of the right side, where surgery had previously seemed urgently indicated, and the transfer of the projected operation to the opposite side, when the appropriate time for it seemed to arrive.

Eventually this was accomplished without mishap. Shortly after the second cystoscopic manipulation the patient passed five calculi varying in size from an English pea to a match head. This largely cleared out the right side for the time being; the shadow on the left remained in situ. Systematic treatment was carried out through a considerable interval, consisting of a general process of upbuilding, wide dilatation of both ureters, and lavage of the renal pelves. During this interval the right side steadily improved, while on the left side the stone shadow slowly but steadily grew. A point was finally reached which appeared to represent the maximum of what could be expected. The area of extravasation on the right side was now reduced to a bead-like excrescence upon the upper ureter; urine from this side still contained considerable pus but the dye output was now two-thirds of normal and the kidney, at first supposedly hopeless, seemed actually ready to shoulder a large load of excretion while its mate underwent the tax of operative removal of its growing calculus. The patient himself was clinically well, at his work daily, robust and the possessor of about forty pounds of new weight. At this time the patient gained entrance to a charity hospital where the stone was removed from the left kidney through a small nephrotomy incision, the pelvis being entirely intrarenal. He was out of the hospital in a little over two weeks and at no time was there the slightest threat of any complication incident to embarrassment of the right side. Three weeks after operation his dye output in two hours was 81 per cent. with 45 per cent. in the first thirty-minute period. At the present time he is apparently in perfect health. A recent X-ray plate shows the left side clear; on the right side there remain a few very small shadows which have persisted throughout. One of these seems to lie just outside the ureter and is probably the stone responsible for the extravasation.

#### SUMMARY

1. Extravasation from the ureter in the absence of external traumatism is an unusual lesion of grave significance, herewith exhibited in three cases.

2. In all three instances the causative factor apparently was necrosis from impaction of a calculus within the ureter.

3. The clinical picture depends upon the amount of extravasation, the virulence of the associated organisms, and the tissue reactions of the patient. Rapidly spreading infection may result or the process may become localized with or without abscess formation.

4. The fact that one of our cases recovered entirely without operative intervention on the affected side is interesting and suggestive.

5. As a rule, however, the condition will be frankly, perhaps imperatively surgical. The time for the application of this surgery, and the type of operative procedure undertaken, will be dictated by the conditions obtaining in the individual case.

## FRACTURES AT THE CONDYLES OF THE FEMUR\*

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IN THE field of traumatic surgery, fractures about the femoral condyles are engaging our attention with increasing frequency. It was the appearance of three such injuries in our wards at the Roosevelt Hospital in fairly rapid succession, which led to an investigation of these cases. The resulting report is based upon thirty-eight cases of fractures at the femoral condyles discovered in the records of the Roosevelt and Lincoln Hospitals over a period of twenty years and ten years respectively.

In 1921, Speed<sup>1</sup> reported but eight cases of condylar fractures in 526 fractures of the femur seen at the Cook County Hospital in three years. Rabut<sup>10</sup> quotes Malgaignes' report of five fractures in the lower third of the femur in a total of 316 femoral fractures. Ashhurst<sup>8</sup> more recently (1926) reported eleven fractures about the condyles in a total of 111 fractured femurs seen at the Episcopal Hospital in Philadelphia.

The fact that these injuries are occurring now more frequently than they did in the past is evidenced by the fact that of the thirty-eight cases here reported seventeen have been seen in the past five years. The cause of this increasing frequency of femoral condyle injuries may be sought in the record of their etiology. Twenty, or rather more than half of them, resulted from automobile accidents—a commentary on the ever-increasing traffic hazards which are filling our accident wards every day. The incidence of these fractures places them in a class with fractures of the skull, the fractures of the tibial head described by Cotton, and with fractures of the pelvis. Most of them, unlike the typical fractures of the radius, clavicle, humerus and femoral neck, are essentially fractures of direct violence and have no predilection for a special age group. The age incidence in the cases here reported is from thirteen months to sixty-four years—an average age of thirty-two—representing a fair mean of the active years. Men were slightly more often the victims than women—25 to 14.

The histories of these injuries are difficult to elicit from the patients. The mechanism is usually vague and can frequently only be inferred from the discovered pathology. The accident itself is so surrounded in the patient's mind by its essential aura of fright, excitement, confusion and pain that little is remembered of its exact character. In a general sense, however, it is apparent from the survey of the mechanism of injury in these cases that direct violence preponderates as an etiological factor. The one exception—that of epiphyseal separation—is noteworthy.

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Another feature of interest in the general consideration of these fractures about the femoral condyles is the frequency with which other injuries are associated with them. Multiple contusions, abrasions and lacerations are the rule rather than the exception, while fractures in other bones or other parts of the femur were present in four of the cases. Shock, too, is a factor very much to be reckoned with in the early treatment of patients suffering these injuries. Sometimes it is extreme, even though the fracture be not

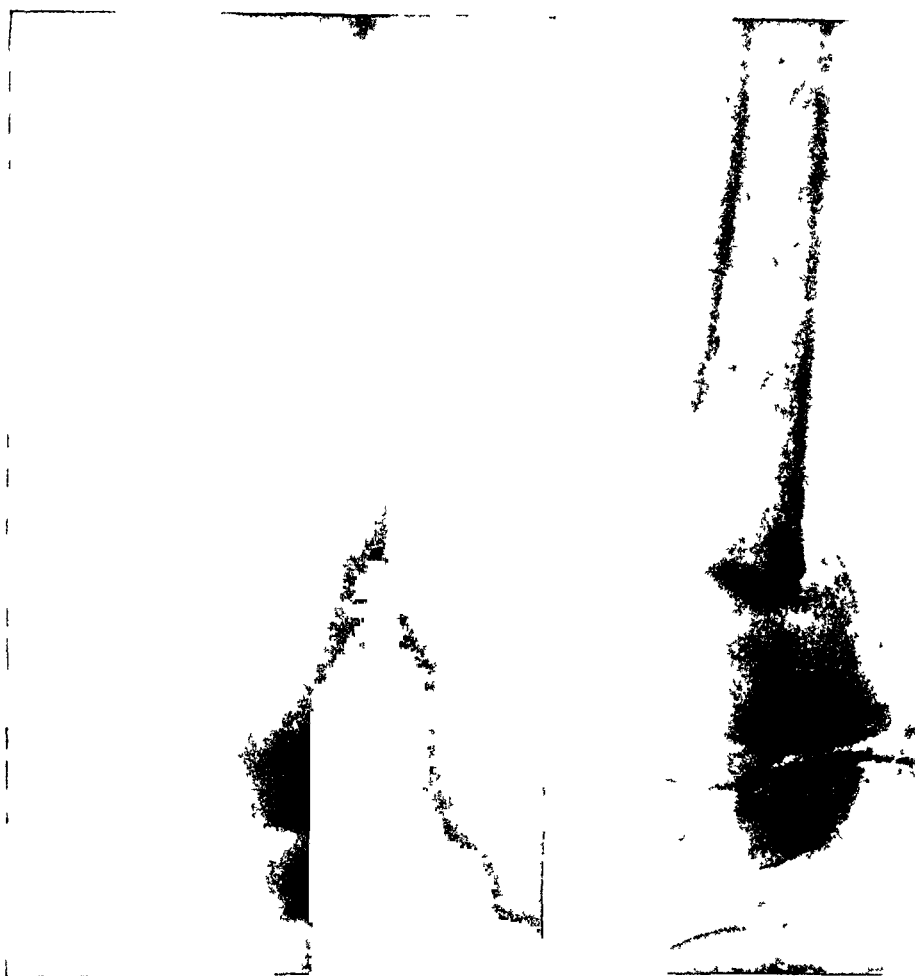


FIG 1—Fracture above the condyles with characteristic posterior displacement

FIG 2—Fracture above the condyles in a child, with anterior displacement

compounded, and requires treatment before attention can be given to the bone injury itself.

For our consideration, these fractures about the condyles may be conveniently grouped in the following classification:

- Fracture above the condyles,
- Fracture between the condyles,
- Fracture of external condyle,
- Fracture of internal condyle,
- Separation of condylar epiphysis.

## FRACTURES AT THE CONDYLES OF THE FEMUR

*Fracture above the condyles.*—(Figs. 1 and 2.) In reading the textbooks and published articles on these injuries, one is left a little in doubt as to just where fractures of the lower femoral shaft end and supracondylar fractures begin. In selecting from our records those cases which should conform most closely to the true supracondylar (such as Moorhead<sup>2</sup> happily describes as juxta-epiphyseal), I have included only the fractures occurring in the flattened portion of the bone, just above the condyles. There were eighteen injuries of this type in the group. The ages of the victims varied from thirteen months to sixty-four years.

As cause of these fractures, our records show that direct violence was almost universally responsible. Ten were struck by automobiles. Two of these were caught between the car or truck and a wall. In one, the legs were run over by the vehicle, both femora being fractured just above the condyles by the wheels. Whether the others injured by cars received their fractures by the impact or by reason of being thrown violently to the knees is uncertain, but one suspects the latter to have been the case. This seems more probable since the bumper of the average car is rather too low to strike the adult femur, and also because six of the cases not injured by cars were hurt by falls upon the knees (two down steps, one from a window, two while walking, one out of bed). One additional patient struck the knee against a tree while coasting. One only of the entire number received this type of fracture by indirect violence. This patient was an arthritic whose femur was recorded as being fractured during an attempt to mobilize a partially ankylosed knee-joint under anæsthesia.

The pathology produced by these injuries showed some variation. Five showed spiral or oblique fractures running up the shaft. Of these, two were oblique in the antero-posterior plane, the others lateral. One of the latter, in a boy of eight years, was oblique into the epiphyseal line and associated with a lateral epiphyseal separation. One of the antero-posterior oblique fractures had a forward displacement of the distal fragment. Ten of the remaining fractures in this group were of the transverse type. Four showed anterior displacement of the distal fragment; the other six the usual posterior position. Oddly enough, the four transverse supracondylar fractures with the atypical forward displacement were in children eight to eleven years old—the deformity corresponding closely to that seen in complete epiphyseal separations. In the adult cases, the posterior displacement, ascribed by Scudder<sup>3</sup>, Speed<sup>4</sup> and others to the pull of the gastrocnemii, occurred with regularity. One of these transverse fractures was of the greenstick type (Fig. 3), occurring in the youngest patient of the group, a baby of thirteen months. The remaining two were compound and comminuted, with crushing injuries of the soft parts.

Complicating injuries with the supracondylar fractures occurred in two other instances besides those noted above. In one, the tibia and fibula were broken in the injured leg. In another the femoral fracture was compound.

In none of the simple fractures was there evidence of injury to the popliteal vessels or nerves, or to the knee-joint.

The clinical appearance of these patients, when admitted, was strikingly similar. All were in a greater or less degree of shock, with prostration and pain. The leg was characteristically helpless, and any movement was attended with great discomfort. Characteristic deformity was usually masked by swelling which appeared early and was in most instances noted as being "considerable" or "marked." Such deformity, as could be observed, suggested a dislocation of the knee. Active and passive motion were restricted because of pain. Marked and diffuse tenderness of the lower femoral

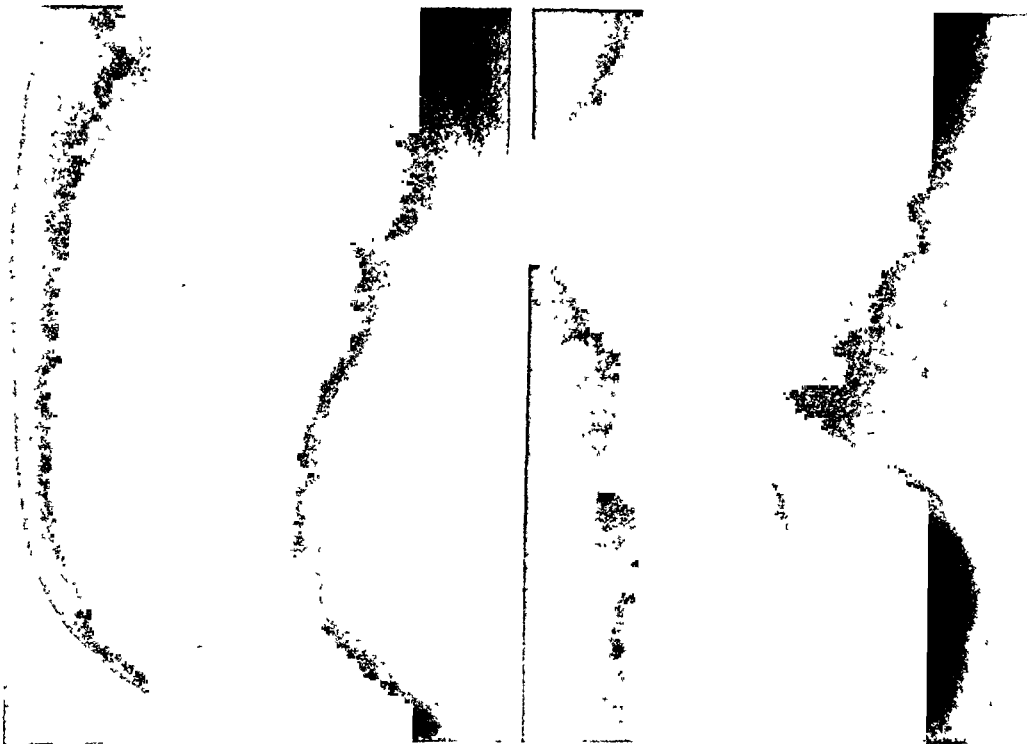


FIG. 3.—Greenstick fracture above the condyles. FIG. 4.—Fracture between the condyles. "T" type.

region was the rule, and precluded satisfactory objective examination. Shortening of one-half to two inches was observed. The diagnosis was confirmed in each instance by X-ray.

The treatment of the fractures above the condyles was by no means uniform in this group. In seven, satisfactory reduction was secured by manipulation, as recommended by Speed.<sup>1</sup> Manipulation to produce these reductions consisted in manual traction, guiding of the lower fragment and flexion. In one instance, where there was anterior displacement of the fragment, resisting reduction, success was attained by flexing the leg against a fulcrum formed by a sling around the upper calf. In six cases, attempts at reduction by manipulation were unsuccessful, and resort was had to traction by various means. This traction was secured by ice tongs in the

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condyles in three instances, and by Steinman pin through the condyles in three. In all but one of them satisfactory reduction was obtained by these means. No open reduction was performed, although it was proposed and refused by the patient in the unsuccessful tong-traction case. This was an oblique fracture with anterior displacement which would not reduce. A fair result was nevertheless obtained. The infant of thirteen months was treated by overhead traction with the legs extended. Three patients received no treatment for their fractures—two who died from shock shortly after admission and one who went home against advice. One other patient had such a severe crushing injury that amputation was necessary.

The fourteen cases treated in this series of eighteen fractures above the condyles responded, with one exception, to one of the two simple means of treatment employed. In those cases where reduction by manipulation was successful and plaster was employed for immobilization, there was encountered no difficulty resulting from pressure or constriction, which Speed<sup>4</sup> cites in warning against its use. Wilson and Cochrane<sup>5</sup> recommend plaster in these cases, while Cotton<sup>6</sup> and Ashhurst<sup>8</sup> prefer Buck's extension and Speed<sup>4</sup> the Hodgen's or Thomas splint.

In the cases where manipulation was not successful, traction with tongs or pin in the condyles proved satisfactory. Perhaps these patients were fortunate in failing to develop any untoward complication in the use of this method. Wilson and Cochrane<sup>5</sup> object to this procedure because of the danger resulting from the insertion of the traction apparatus so close to the fracture. There has seemed to us, however, a certain advantage in applying traction at the condyles, rather than at the tibial head as suggested by Moorhead<sup>2</sup> or at the calcaneus as Speed<sup>4</sup> recommends, in that the distal fragment may be more accurately controlled. This is a matter of some importance, because of the difficulty in overcoming the backward displacement and rotation of the distal fragment which is so characteristic and frequently so stubborn. In fact, the higher the tongs or pin can be inserted, below the fracture, the better for the purpose of mechanical reduction.

Our experience in handling these cases with traction convinces us of the desirability of a position of the leg in which the hip and knee are both flexed. On this point, most of the authorities consulted seem to agree. To accomplish this, we have found the suspended Thomas splint with Pearson attachment entirely satisfactory. This is employed with direct traction on the condyles, exerted through the tongs, supplemented with light traction on the lower leg through adhesive strips on the skin. This latter force aids materially, it seems, in tilting the distal fragment forward. These pulls may be varied in direction and force to accomplish the desired end.

Following reduction, and a period of retention either in plaster or splint over a period of from six to eight weeks, these patients were allowed up with crutches and were given physiotherapeutic treatment.

As to the results to be expected in fractures above the condyles, Speed<sup>4</sup> is not very optimistic. Pointing out the difficulty of securing and maintaining

reduction and the likelihood of persisting stiffness, he declares the prognosis for full function poor. Cotton<sup>6</sup> calls the prognosis fair, while Ashhurst,<sup>8</sup> reporting six supracondylar fractures in a series of eleven fractures of the lower femur, had one fully satisfactory result.

Of this group of eighteen cases, the results are recorded on the following data:—

|   |   |
|---|---|
| Left hospital at own request.....                           | 1 |
| Died within three hours of admission.....                   | 2 |
| Leg amputated for irretrievable crushing injury.....        | 1 |
| Not seen after discharge .....                              | 5 |
| Result observed by follow-up (six months to ten years)..... | 9 |

Of those not seen after discharge, four left the hospital with satisfactory early results; *i.e.*, with union, no deformity, no shortening and returning function. One case had three-quarters inch shortening and slight posterior angulation. What the eventual results may have been in these cases, we have been unable to determine. Of the nine cases followed subsequently to their discharge, for periods varying from six months to ten years, four satisfactory and five poor results were noted at the time of leaving the hospital, while the late results were reported satisfactory in six, and poor in three. The satisfactory results had good union, no deformity, no shortening and good function. Of the poor results, all had one-half inch to three-quarters inch shortening with some limp. All of the five in which a late satisfactory result was reported had been treated by closed reduction and plaster. Of the three poor results, all had been treated with Steinman pin or tongs and traction. The difference here, it seems fair to assume, depends primarily on the original nature of the fracture (as suggested by the treatment required), rather than on the type of treatment.

*Fracture between the condyles.*—Closely allied to the fracture above the condyles, because always accompanied by it, is the fracture between the condyles. In fact, Scudder<sup>3</sup> groups these fractures together in his discussion of them. Yet it seems that they should be classified separately because of one important point of difference. The fracture between the condyles inevitably involves the knee-joint, introducing a difference in pathology, in prognosis and new problems in treatment. Also, fortunately, it is distinctly less frequent in occurrence.

In this group of thirty-eight cases of fractures about the condyles, there were but seven of the intercondylar type. All but one occurred in patients from forty to forty-five years of age. The exception was eighteen.

As in the case of most of the fractures above the condyles, these injuries were produced by direct violence. Our experience here agrees with that of Cotton<sup>6</sup>. Five followed violent falls on the knee; one patient was hit by a truck; while one occurred in an automobile collision.

The pathology, as observed in these cases, was quite similar. All were of the T-type. Six had transverse fractures above the condyles (four with typical backward displacement), and the other a spiral fracture separating

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the condyles from the shaft in addition to the intercondylar injury. No instance of the Y-fracture with wide separation of the condyles was seen. Marked effusion into the knee-joint and hæmarthrosis were present in all.

Complications, too, were relatively common. One patient presented a comminuted fracture of the patella in addition to his femoral injury. In one case, the shaft of the same femur was broken in the middle third, and a fracture of the radius on the same side had been sustained. Two of the others were compound.

In six of the cases, the clinical aspect shortly after injury was typical. Shock, pain and disability were the prominent characteristics. Marked swelling about and above the knee was present, with tenderness and a curious feeling of "looseness" on palpation, with separate mobility of the condyles. The exact nature and extent of the injury was found difficult to estimate without the aid of the X-ray. One case presented a striking difference. This man had fallen on his knee a month before admission and came complaining of stiffness and some pain and lameness in walking. Examination showed some tenderness about the condyles and fluid in the knee-joint. The leg was held somewhat flexed, the motion being much limited. The X-ray demonstrated a T-fracture without displacement.

This patient, in the way of treatment, was kept in bed for a week, had physiotherapy for three weeks, and then, the knee remaining quite fixed in semi-flexion, it was straightened under ether, and a cast applied in the extended position. With the others, it was a different story. One of the compound fracture cases was treated by suspension and skin traction in a Thomas splint for five days. A gas bacillus infection of the wound then occurred, necessitating amputation. Death ensued. The other compound fracture was recorded as being treated with similar traction for three days. No reduction being obtained, traction by a pin in the tibial head was substituted for thirty days. Some improvement of position was obtained but no union. An ambulatory pneumatic splint was then tried with the same result. Then open reduction was done. This was followed by sepsis, amputation and death. Two of the remaining cases, not compounded, were successfully treated with skin traction and subsequent application of plaster in extension. The patient with the complicating mid-third fracture of the femur was treated by traction applied through hooks inserted in a plaster cast which extended from the toes to mid-thigh. A satisfactory reduction and maintenance of both fractures was thus obtained. In one case, where skin traction proved inadequate, direct traction was applied with ice-tongs in the condyles.

It is apparent, even from these few cases, that in this type of fracture, involving the knee-joint, the hazards of infection are particularly great. A compound fracture of this kind must be looked upon as a grave injury. In addition, it would seem unwise to institute any therapeutic measures which might conceivably introduce infection. Hence, aspiration of the knee-joint



has been avoided, although tongs were inserted in one case. Hitzrot<sup>9</sup> stresses this point in speaking of the dangers of using Steinman pin or tongs in the femur in this type of injury. This risk would apply also to open reduction, although Scudder<sup>3</sup> suggests that these fractures are best treated in the adult by direct reposition by operation, especially if after putting the leg "in a position of physiological rest and relaxation," "with or without traction as may seem wise" for six days, the reduction secured is imperfect. Speed,<sup>1</sup> too, suggests open reduction through the knee by splitting the patella and fixing the fragments with nail or screw, although he says that bicondylar fractures are "best treated" by strong, continuous traction in semiflexion. Cotton,<sup>6</sup> on the other hand, recommends reduction under ether, pressure on the condyles and Buck's extension. He says, "I know nothing of the operative treatment of these cases." "One would rather not operate if operation could be avoided with fair prospects." In the uncomplicated cases, such as three in the group here reported, treatment by skin traction with subsequent application of plaster with the knee in the extended position has sufficed. In the presence of stubborn posterior displacement of the fragments, traction on a pin through the upper tibia, as recommended by Wilson and Cochrane<sup>5</sup>, might be resorted to. In all of these measures, the pull on the lateral ligaments of the knee is depended upon to approximate the separated condyles, aided, perhaps, by direct lateral pressure on the condyles themselves.

In the cases here considered, the plaster was left on, following reduction by traction, for periods varying from three to six weeks. Massage, active and passive motion were then begun. While recognizing the advantages of early motion, there was a distinct disinclination to jeopardize the union before it was solid. The use of Thomas splint and Pearson attachment would no doubt permit earlier motion at the knee with less risk of malunion.

Three of the five cases reported here could not be traced, although at the time of discharge they were noted as having satisfactory union with returning function. The third case (the one in whom the fracture presented minor signs) reported a good result, as might as been expected, at follow-up. The case with double fracture had some limp and one-half inch shortening.

*Fracture of internal condyle* (Fig. 5).—This fracture occurred three times in the thirty-eight cases here reported. Although it, too, involves the knee-joint directly and may, as Wilson and Cochrane<sup>5</sup> point out, interfere with the subsequent function by reason of displacement of part of the joint surface, it is in no respect as severe an injury as the discondylar break.

Speed<sup>4</sup> observes that these injuries may come from direct violence—crushing—or from indirect, by upward thrust of the tibia, as in falls on the feet from a height, or from twists. Cotton<sup>6</sup> suggests forced adduction or abduction as the cause. In one of our cases, the nature of the trauma was not recorded. Both of the others fell downstairs, one with a beer-barrel which rolled over his leg. Thus one may have been due to a twist or to direct violence, while the other was almost certainly direct.

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All three fractures occurred in patients of middle age.

The pathology of these cases, as demonstrated by X-ray, varied but little. Two were longitudinal in character, separating the inner condyle from its fellow and from the shaft with slight upward displacement. The other was oblique, through the inner condyle, the distal fragment being rotated backward, pretty effectually locking the knee-joint. This latter was the one produced by direct violence.

This particular patient had not recovered sufficiently from his encounter with the beer-barrel to appear at the hospital until four weeks later. At that time, he had a very stiff and swollen knee which was tender on its inner aspect and practically immobile in semiflexion. The others presented on admission painful and swollen knees with localized tenderness over the

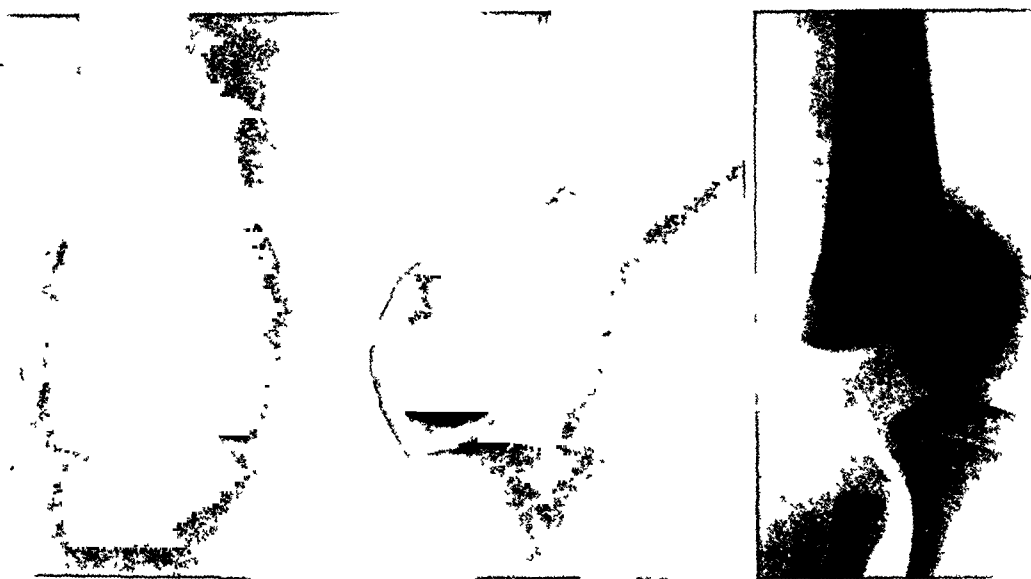


FIG. 5.—Fracture of internal condyle.

FIG. 6.—Fracture of external condyle.

FIG. 7.—Separation of condylar epiphysis.

injured condyle, signs of fluid in the joint, false motion of the fragment and restriction of function by pain.

Treatment in each instance consisted of reduction under full anaesthesia with replacement of the fragment in its proper position by restoring the axis of the leg and pressure on the fragment, as Cotton<sup>6</sup> advises. The legs were immobilized in plaster for from four to six weeks. No open reduction or nailing of fragments was necessary (few cases require it, according to Speed<sup>4</sup>), nor were any of the fragments removed.

Satisfactory progress was noted on these three cases at the time of discharge. Unfortunately, none of them could be traced at recall.

*Fracture of external condyle* (Fig. 6).—Five fractures of the external condyle were found on our records, showing a slightly greater relative frequency than those of the internal. As in the former group, all these were in adults, from twenty-four to forty-five years of age.

All but one were apparently produced by direct violence. Two patients

fell on the knees. One struck his knee against a curbstone. One had a heavy block of stone fall on the knee. The one in which the nature of the trauma was uncertain was struck by an automobile.

This latter patient had a chip fracture of the epicondyle. Two of the others showed longitudinal and two oblique fracture of the condyle, all involving the knee-joint. All showed a greater or less degree of upward displacement and slight backward tilting of the fragment on X-ray examination.

The picture presented by these patients closely resembled that shown by those suffering from internal condyle fractures, in so far as disability, pain, swelling and fluid in the knee-joint were concerned. The tenderness was most marked over the external condyle. In two, a definite genu valgus was observed. One patient, in spite of slight displacement of the fragment, had been able to walk home following his injury.

The chip fracture case required only immobilization in plaster for one week. One case, with some displacement, left the hospital soon after admission and was lost track of. The other one in which displacement was present was given skin traction for two weeks. Reduction being unsatisfactory, tongs were applied and left in place for three and one-half weeks longer—a questionable procedure. Good reduction and union, however, were obtained. The two cases showing little or no displacement were merely kept in bed for four weeks. This, where the conditions warrant, is an ideal treatment. It obviates displacement from weight-bearing during the period of union, and, owing to the freedom of the knee, promotes early restoration of function. In one of these cases, aspiration of the knee was done without ill effect.

Both of these cases obtained satisfactory late results, as did the chip fracture case. The patient with displacement was discharged from the hospital at ten weeks with good union, no deformity and motion 50 per cent. restored.

*Separation of condylar epiphysis* (Fig. 7).—Epiphyseal separation of the femoral condyles, the apparent response of the juvenile to trauma which, in the adult, may cause condylar or supracondylar fracture, occurred in the group here reported five times. All instances occurred in children of five to eleven years of age.

The accident to which these injuries are classically ascribed—severe twisting of the leg, as when caught in the spokes of a revolving wheel—accounted for two of the group. Cotton<sup>6</sup> says that this injury is usually caused by strong hyperextension, the posterior ligament pulling free the epiphysis. Two of these separations were caused by the patients being struck by automobiles. The fifth was produced by a car running over the leg, fairly definite evidence that direct injury may be the cause in some cases. Speed<sup>4</sup> verifies this in his observation that a direct blow on the lower thigh or knee may be responsible.

The typical displacement of the distal fragment forward was observed in all of these cases but one. In this instance (one of the injuries produced

by twisting), the displacement was outward, the diaphysis having torn and penetrated the vastus externus. The patient run over by a car had some lateral as well as anterior displacement. No complicating injuries of moment were observed in any of these patients, except one, where paralysis of the external popliteal nerve occurred.

Shock was not a marked feature of these cases. The injured legs showed the characteristic deformity with anterior bowing above the knee and obliteration of the popliteal space. The case with laterally displaced epiphysis strongly suggested dislocation by its appearance. In all there was tenderness above the knee, but no evidence of fluid in the joint. Motion in the knee-joint was not greatly restricted. False motion at the site of injury could be elicited in but one instance. The diagnoses, while confirmed by X-ray, were not especially difficult to differentiate from dislocation, because of the unaltered relations of the structures comprising the knee-joint.

Treatment of these cases presented some difficulties. The usual method of reduction, traction upon the leg with the knee bent and manipulation of the distal fragment, under anæsthesia, was attempted in all. It was fully successful in but two of the five injuries. These, following reduction, were maintained in flexion by plaster dressings. In one of these, subsequent straightenings of the knee under ether were necessary to overcome fixed flexion. Of the unsuccessful reductions, one slipped, when, at the end of four weeks, extension was permitted, requiring a second manipulation and subsequent immobilization in extension. The case with lateral displacement could not be reduced by the closed method, and open replacement was resorted to. The same was true of the fifth case. Here the always dreaded infection supervened, producing a septic arthritis of the knee and eventual ankylosis.

The experience in the treatment of the cases of epiphyseal separation here recorded, therefore, has led us to consider these injuries with some trepidation. The reduction is by no means always as simple as it looks, and when once achieved may be difficult to maintain. Open reduction, possibly with fixation either from the shaft or joint side by nailing, as suggested by Speed <sup>4</sup> in the difficult cases, seems hazardous. The sling-fulcrum manœuvre, successful in one of our cases where manual reduction had failed, might prove helpful, or traction with Thomas splint and turnbuckle applied at the ankle. One might almost be tempted to try slower weight traction with a pin low in the tibial head before resorting to operation. We have had no experience with the latter method.

The results obtained in the five cases here considered were hardly brilliant. One, as indicated, had a permanently stiff knee. The other patient, upon whom open reduction was done, secured a perfect result. So also did the two cases in whom successful closed reductions were performed—one of them in spite of early external popliteal nerve paralysis. The remaining patient left the hospital with cast still applied, and no follow-up

record is available. Thus three satisfactory results out of five cases is the score for this group of epiphyseal separations.

SUMMARY

|                            | Number | A. O. R. | Result       |                |              |                |
|----------------------------|--------|----------|--------------|----------------|--------------|----------------|
|                            |        |          | Early Only   |                | Late         |                |
|                            |        |          | Satisfactory | Unsatisfactory | Satisfactory | Unsatisfactory |
| Above condyles.....        | 18     | 1        | 4            | 4              | 6            | 3              |
| Between condyles.....      | 7      | —        | 2            | 3              | 1            | 1              |
| Internal condyle.....      | 3      | —        | 3            | —              | —            | —              |
| External condyle.....      | 5      | 1        | 1            | —              | 3            | —              |
| Separation of epiphysis... | 5      | —        | —            | 1              | 3            | 1              |
| Total.....                 | 38     | 2        | 10           | 8*             | 13           | 5              |

\* Including deaths and amputations.

The study of this group of fractures about the condyles has demonstrated to us certain salient features concerning them. We are reminded afresh of the seriousness of this type of injury, not only as regards its menace to future usefulness of the limb, but even to the life of the patient. One has been impressed with the difficulty which proper reduction and maintenance of the fragments entail. Also, it is apparent that, even in each of the several classes of fracture here met with, there is no one method applicable to their treatment. Certain general principles being accepted, each fracture presents a unique problem of its own upon which the surgeon must bring to bear his judgment and ingenuity. One cannot but be impressed, too, with the gravity of infection in these cases and, because of this danger (particularly where the knee-joint is involved), prefer to attempt every available means of securing reduction before resorting to operation. The results obtained leave much to be desired, and invite, therefore, further investigation of these injuries with a view to improvement in their management.

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# FRACTURE OF THE SHAFT OF BOTH BONES OF THE LEG\*

AN ANALYSIS OF 107 CASES

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FROM THE SURGICAL SERVICE OF THE BEEKMAN STREET HOSPITAL

LITTLE has been published in the past few years regarding the treatment and result in fractures of both bones of the leg, not involving the joints. I am offering nothing new in the way of treatment, but wish to bring for consideration one hundred fourteen consecutive cases treated by the staff of the Beekman Street Hospital during the six-year period from 1924 to 1929, inclusive. This hospital is located in the downtown district of New York City, which is a section of high buildings, incessant new construction and intense traffic congestion. In our ambulance district there is said to be a resident population of only thirty thousand people and a working population of seven hundred fifty thousand. This explains the age and sex groups and the type of fracture which appear in this analysis. We have not insisted on any one method of treatment, but are partial to traction suspension treatment by means of the Steinman pin through the os calcis in cases of overriding. There are still many horses present in the district where we work, hence gas bacillus infection is prevalent and we do not feel justified in open operation as a routine procedure. Also, we believe that traction suspension gives satisfactory results, is less dangerous, and causes no particular lengthening of the period of the patient's disability. Many of our cases are compounded and such treatment is more rational in these than immediate application of plates or screws, as is frequently recommended.

The treatment given the patient immediately after the fracture occurs is the all-important one. Our ambulance surgeons are instructed to apply a Thomas splint to all these patients where they lie, whether on the street or in a building. The clothing is not removed, but cut when necessary for the dressing of wounds and tentative diagnosis. Traction is obtained by a hitch about the ankle. Morphine is administered as a routine. All fractures are emergency cases about which the visiting surgeon must be immediately consulted. In the emergency room, traction is removed only long enough to determine the site to be X-rayed and then is immediately reapplied. Examination for crepitus and false point of motion is made only when necessary to determine the part to be X-rayed. In compound fractures, tetanus antitoxin is given in the emergency room. The presence of shock is decided by the resident surgeon, and, if present, its treatment is commenced here. If the patient's condition warrants, he is next taken to the X-ray room for a picture. He then goes to the ward, where removal of his clothes is supervised so that

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\* Read before the New York Surgical Society, October 22, 1930.

manual traction on the extremity will be maintained if the hitch has to be loosened. The emergency traction is inspected at least every half hour to guard against circulatory embarrassment, and this traction remains on until the final treatment has been decided upon, after inspection of the X-rays.

Compound fractures are thoroughly scrubbed, irrigated and débrided as soon as the patient's condition warrants anæsthesia. Anæsthesia is used for practically all manual reductions. Steinman pins are inserted in the ward if it is felt that the patient's condition is such that he should not be removed to the operating room.

To summarize, we find that fracture of the shaft of the long bones is frequently a shocking injury. This shock is combated by morphine and care against submitting the patient to further movement of the fragments, pain, *etc.* Also, putting the muscles at rest by immediate traction does more to facilitate proper reduction than any other single procedure.

If there seems to be any likelihood that a manual reduction can be obtained and maintained, this is always attempted first. Plaster splints are then applied. Circular supports are not allowed in early treatment, but we use posterior and lateral sugar-tong splints of molded plaster extending from mid-thigh to toes with the knee in slight flexion and the foot at right angles and somewhat inverted. The fluoroscope is used during reduction as occasion demands. In the markedly oblique fractures or in those in which overriding is present after attempted manual reduction, the Steinman pin is inserted through the middle of the os calcis. The solid type of pin is used. Fifteen pounds of traction are ordinarily applied for a few hours and reduced to ten pounds when the proper length has been obtained. Skin traction may be effective in fractures of the upper third, but we have not been satisfied with it in the lower two-thirds, as more weight is required than the area of available skin will tolerate for pull. Ice tongs in the malleoli have been used in some cases, but for some time past we have discarded them as they were prone to penetrate too far or to slip.

Open operation is reserved for those patients in whom satisfactory reduction cannot be obtained by the above methods or when it is believed that there is tissue between the fragments.

As Gilcreest<sup>1</sup> says, every effort should be made toward obtaining the normal axis of the leg, *i.e.*, the longitudinal axis of the main fragments of the tibia must be parallel, but some lateral displacement will not interfere with perfect function. A line drawn through the centre of the long axis of the shaft of the tibia should also bisect at right angles a line through the horizontal axis of the astragalus.

For purposes of analysis, I have divided these cases into four groups, *viz.*, spiral fractures, fractures of the upper third, the middle third, and the lower third.

**SPIRAL FRACTURES.**—These most commonly involve the tibia in its distal half and the fibula in its proximal half.

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In this group there were twelve male patients and one female patient. Seventy-seven per cent. were between thirty and fifty years of age.

All of these injuries were by indirect torsion violence, except possibly in the case of one man who claimed that while he was drunk he was kicked in the leg. The typical histories were: "Fell while climbing a ladder and leg caught between rungs"; "Fell ten feet, landing on feet"; "Leg caught between two plates of plow"; "Caught between gang-plank and hand truck and thrown to ground."

Eleven were simple and two were compound fractures. The two compound fractures were apparently compounded from within, *i.e.*, a small punctured wound was present over a sharp fragment. The wound was irrigated but no débridement was done. Four were comminuted fractures, all in the



FIG. 1.—Case No. 6064. Spiral fracture before and after reduction. Treated in plaster splints.

fibula only. Two were complicated by other injuries which prolonged the patients' stay in the hospital. No. 3921 A was a fracture of the os calcis, with operation and post-operative infection. No. 4649 was kept in the hospital on account of an eye lesion which required enucleation.

*Treatment.*—In three patients the position was such that posterior and sugar-tong molded plaster splints were applied without any manual reduction. In three others manipulation was done without anæsthesia and plaster was applied. Four were reduced under general anæsthesia and plaster was applied. One had traction by Steinman pin and two had traction by ice tongs as their first treatment. In three of the reductions there was later slipping of the fragments, one patient having tongs inserted in the malleoli on the third day, one having an open operation with Lane plating on the tenth day and one having a Steinman pin inserted through the os calcis on the



twentieth day. That is, out of seven cases in which manual reduction was necessary and attempted, three were unsuccessful. The three cases in which ice tongs were used were in January, 1927, or before. At present the Steinman pin is being used for such cases. In the three unsuccessful reductions, anæsthesia had been used once and none twice. In each case the X-ray showed that the fragments had slipped. To summarize, out of ten cases that required any manipulation, six had to have either traction suspension or open operation. It is a question whether simple application of plaster is not a waste of time in these cases.

The ice tongs or pin were removed at periods from twenty-six to fifty-five days after injury with an average of thirty-nine days. On removal of ice tongs or Steinman pin, adhesive plaster traction suspension was instituted in one case, and in the other four, plaster splints were applied. In one patient the tongs slipped and were removed on the twenty-ninth day when it was felt that there was sufficient callus to hold the fragments in position. The leg was left in suspension without traction and on the forty-first day union was clinically firm and the patient was allowed up in a chair. Definite separation of the tibial fragments then appeared and increased progressively so that on the fifty-fifth day an open operation was done and fascia was removed from between the bone ends. Only fair opposition could be obtained and two kangaroo-tendon sutures were placed through the bone. Union was solid at twenty-six weeks. I believe this patient suffered from insufficient immobilization in all the methods of treatment tried.

In those cases in which tongs or a pin were used, ten pounds' traction were sufficient for those who had this method instituted immediately, and fifteen, later reduced to ten, on those on whom it was applied after the first twenty-four hours. There was no difficulty about the healing of the wounds in any case. There was but one child in this group, nine years old, treated in plaster splints.

We know that all these patients obtained solid union, although we do not know the exact time in all. It is often mentioned in the X-ray report that callus might have been demonstrated if the leg had not been in plaster splints. The presence of callus was not mentioned in one case. It was mentioned for the first time as being present in six cases at a period varying from twenty-five to ninety-one days with an average of forty-nine days and without one long case, forty-one days. On the last X-ray taken while in the hospital, it was mentioned that there was no callus present in six cases. These varied from twenty-six to seventy-five days with an average of forty days, or without the one delayed case an average of thirty-four days. In other words, callus seems to appear most commonly in the sixth or seventh week. The patient who showed no callus at seventy-five days had solid union at ninety days, the false point of motion being only slight at forty-five days. On the other hand, the patient showing callus at twenty-five days had to be operated upon at fifty-five days and fascia was found between bone fragments.

The presence of firm union was mentioned in the notes of nine patients.

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By firm union we mean that considerable effort is necessary to obtain a false point of motion in any direction. The time varied from twenty-six to ninety-eight days with an average of fifty days. Solid union was mentioned seven times, occurring at periods varying from fifty-six to one hundred fifty-four days, an average of eighty-four days. One patient was discharged at one hundred fifty-four days with a false point of motion still present, even though he had shown firm union at fifty-six days. He was treated in plaster splints and obtained solid union ultimately.

The cases on whom skeletal traction was used were the more difficult ones. Here the average time for firm union was fifty-nine days and for solid union ninety days. This included the unsuccessful case of a patient who later had an open operation for removal of fascia from between the fragments. He had solid union five and one-half months after injury. Omitting this case from the summary, solid union was obtained in the patients treated only with plaster in an average of seventy-five days and in those with skeletal traction in sixty-nine days. At least, there is no evidence that skeletal traction prolonged the period of disability.

In recording our results I have used the Massachusetts General Hospital method of rating.<sup>2</sup> The letters A, E, and F signify anatomic result, economic result and functional result, respectively. The figures 1, 2, 3 and 4 after each letter give the percentage value to the final estimation, allowing a range of twenty-five per cent. for each figure, *i.e.*, 1—25 per cent., 2—50 per cent., 3—75 per cent., and 4—100 per cent. Various factors are concerned in arriving at each figure. These are fully described in the above reference. The economic and functional results are estimated after one year.

Six had practically perfect anatomical reduction. Five more had slight angulation or dishing but would come under the Massachusetts General Hospital rating of A<sup>4</sup>. Of the other two, one is A<sup>3</sup> and one A<sup>2</sup>, both F<sup>4</sup>.

No. 4676, A<sup>3</sup>.—Dishing of 10 per cent. with overriding of less than one-half inch after late open operation with insertion of two kangaroo-tendon sutures.

No. 6412, A<sup>2</sup>.—One-inch shortening. Upper fragment of tibia displaced medially, almost full diameter of bone. Function normal.

In only three was there appreciable shortening, *viz.*, less than three-eighths inch, one-half inch, one inch as end-result. The first of these was treated by Steinman pin and the last two by tongs, which slipped in each case.

Of the thirteen patients we have obtained the late result at one year or more in five cases. According to the Massachusetts General Hospital rating, three of these were A<sup>4</sup>, E<sup>4</sup>, F<sup>4</sup>, *i.e.*, the best possible result anatomically, economically and functionally. One patient had A<sup>4</sup>, F<sup>4</sup> at one year, but was intensely neurotic and would not return to work and must be given E<sup>0</sup>. The last of these five patients had A<sup>3</sup>, E<sup>4</sup>, F<sup>4</sup>. He had shortening of less than one-half inch and an angulation of ten degrees at site of fracture. The only datum I have been able to obtain on one other patient is that he returned to his accustomed work in five months.

The three patients who were A<sup>4</sup>, E<sup>4</sup>, F<sup>4</sup> were respectively a compound fracture treated in plaster splints, an open reduction with Lane plating, and a Steinman pin case. The A<sup>3</sup>, E<sup>4</sup>, F<sup>4</sup> patient was treated by ice tongs with a later open reduction for interposed fascia. The A<sup>4</sup>, E<sup>0</sup>, F<sup>4</sup> patient was treated by Steinman pin and the patient who returned to work at five months by ice tongs.

Rixford<sup>3</sup> believes that spiral fractures should have an open operation. He states that results by reduction and fixation or by traction are unsatisfactory anatomically and functionally, that non-union is frequent, and that, in case of union, irregularity of the bone is the rule with persistence of lateral rotation of the leg in the majority of cases and with frequent anterior flexion deformity and more or less shortening. This has not been our experience. We believe open operation is an acceptable method of treatment in proper surroundings and in suitable hands. At Beckman Street Hospital, where there are many dirty cases and where the district is prone to contaminations causing gas bacillus infections, the routine use of traction is much safer. We believe that our late results compare favorably with results by open operation. Neither can we subscribe to the ideas of those who believe that moderate shortening can be disregarded as long as the fragments are in the proper axis. Traction will overcome this shortening and not add appreciably to the hazards. If there is any overriding, it is questionable whether any reduction should be attempted before traction is instituted.

UPPER THIRD.—There were nine patients in this group, seven male and two female. None was under fifteen years of age, six were between the ages of sixteen and forty, and three were over fifty.

Six had simple fractures and three compound. Fractures in this area seem to be characterized by frequent comminution, as there were seven in this series. Three were apparently caused by direct and six by indirect violence, but this may not be correct as six were automobile accidents and the patient's story of the mechanism of injury may not have been accurate. All the compound fractures were by direct violence, *i.e.*, compounded from the outside.

Three cases were complicated by other injuries, none of which necessitated the prolongation of their stay in the hospital.

No. 5305 had a fracture of the twelfth dorsal vertebra and the second lumbar vertebra.

No. 5991 sustained a dislocation of the shoulder.

No. 12474 had concussion of the brain.

*Treatment.*—In only one patient was an attempt at manual reduction made. This was simply a molding of fragments without anæsthesia. Five patients had posterior and lateral molded plaster splints applied with satisfactory position in all. The Steinman pin through the os calcis was used on three patients, in two because of greater ease in dressing severe compound fractures, and in one, with very marked comminution, in an attempt to improve the position of the fragments. This last patient was suffering from cerebro-spinal syphilis and became so irrational that he was transferred to Bellevue

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Hospital on the twenty-fifth day, the traction being removed and the leg encased in posterior and lateral molded plaster splints. Of the other two, one had a disarticulation through the knee-joint on the fourteenth day for gangrene following posterior tibial embolism. The remaining patient had the pin in until the seventy-second day, when adhesive plaster traction was substituted and continued until the one-hundred-twenty-first day. One patient had adhesive plaster traction for thirty-five days and the leg was then placed in plaster splints.

Presence of callus was not mentioned in two cases and one patient had an

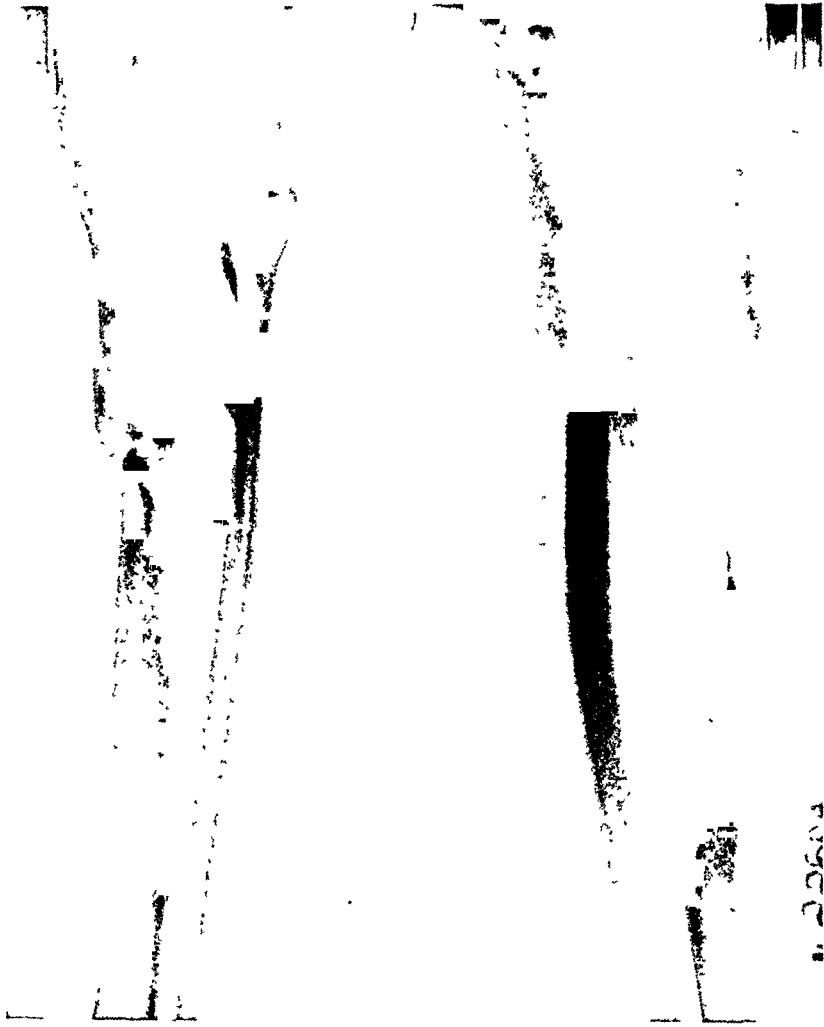


FIG. 2.—Case No. 10034. Marked comminution of tibia in fracture of both bones, upper third. Thirty-five days after injury this shows considerable callus.

amputation on the fourteenth day. In three the X-ray reports mentioned that there was no callus present at twenty, twenty-five and fifty days. One picture showed a fair amount of callus at eighty days but there had been no picture taken since the twentieth day; another showed considerable callus at sixty days, but no picture had been taken since the second day. A boy of sixteen showed considerable callus on the thirty-fifth day. No conclusion as to the average time of callus formation can be drawn from such a small series.

The time of expected union cannot be determined from this series. Two patients had to be transferred to another hospital before sufficient time had elapsed for evidence of union. One patient had an amputation on the fourteenth day. In one case union is not mentioned, but the patient was bearing weight in plaster splints at forty-six days. In four cases union is mentioned as fairly firm in twenty-two, thirty-two, thirty-five and one hundred seventeen days. Solid union was obtained in forty-five, sixty-three, eighty, ninety, and one hundred ninety-six days, respectively. Omitting the delayed case, the average period before solid union was seventy days. The patient who had solid union in forty-five days was sixteen years old. The delayed case presented many complications—a man, aged sixty-six, with a severe compound comminuted fracture requiring extensive débridement of skin and muscles. Gas bacillus infection appeared on the fourth day. The area was incised widely and tetanus perfringens serum given. The patient was in bad condition for ten days, sloughing away a great deal of tissue. On the sixteenth day sugar appeared in the urine and was not gotten completely under control for three weeks, by which time the wound was covered with clean granulations. Up to the sixty-third day there was exposed bone in the wound. The wound then was covered by granulation and on the sixty-fourth day Thiersch grafts were applied to the large open area. All grafts were successful. Traction, as said before, was continued up to the one-hundred-twenty-first day, when splints were applied and the patient was allowed up in a chair. He was discharged from the hospital after seven and one-half months, walking with a cane. He had solid union. A small granulating area was present with evidently low-grade bone infection beneath. At thirteen months two small sequestra came away and the wound promptly healed. At fifteen months the patient showed some modification of gait and a slight deformity.

*Complications.*—*Gas bacillus infection*, one.

*Amputation for posterior tibial embolus*, one.

*Nerve injury*, two.

The patient with fracture of two vertebræ showed nerve injury causing loss of power of flexion and extension of foot on the side of the leg fracture, hypæsthesia and loss of muscle tendon sense in the toes. At fifteen and one-half months he showed slight weakness in dorsiflexion at ankle only. He remained in the hospital eight and one-half months. One patient showed signs suggesting peroneal nerve injury at four weeks, but was entirely normal at discharge on the eighty-second day.

*Psychosis*, one.

*Delirium tremens*, one.

*Late result.*—We do not know the final result in the two cases transferred to other hospitals. One patient had an amputation. All the others obtained solid union. One patient had A<sup>2</sup>, F<sup>3</sup> (nerve injury involving foot) at fifteen and one-half months, but E<sup>0</sup> being still under treatment for two fractured vertebræ.

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No. 5305, A<sup>2</sup>.—Angulation of thirty degrees at a level two inches below knee, so that shaft below is displaced medially. Treated in plaster splints.

One patient had A<sup>4</sup>, F<sup>4</sup> at fifteen months but had not returned to work. He had been confined to the hospital for seven and one-half months and inasmuch as he was sixty-seven years old when last seen and had been a laborer he probably did not return to work. The sixteen-year-old boy returned to his customary work at three months, A<sup>4</sup>, E<sup>4</sup>, F<sup>4</sup>. The result after one year we do not know in the remaining cases.



FIG. 3.—Case No. 6398. Compound fracture of both bones, middle third, with overriding. In insufficient temporary traction.

Apparently, one does not need to concern oneself about non-union in fractures of the upper third, but the incidence of complications is large in our series. Simple immobilization in plaster splints seems satisfactory except in complicated cases where traction suspension is valuable.

MIDDLE THIRD.—In this group there were thirty-five patients, of whom thirty-four were male and one female. Their ages were as follows: 0 to 15 years, 3; 16 to 29 years, 12; 30 to 39 years, 7; 40 to 49 years, 5; 50 to 59 years, 8.

Twenty-four were simple and eleven were compound fractures. Five were apparently compounded from within and six from without. Twenty-two,

or almost two-thirds of the group, were comminuted. Twenty-five were apparently injuries by direct and ten by indirect violence. Eleven were caused by automobile accidents, ten by being struck on the leg by a heavy object and four by falls from a height.

Four patients had other injuries.

No. 3528 had a fracture of both bones of the upper third of the forearm.

No. 8098 had a fracture of the shaft of the femur, middle third, comminuted.

No. 11063 sustained a fracture of the femur, the fifth metatarsal bone, the middle phalanx of the fifth toe, dislocation of the phalanges of the fifth toe and the distal phalanx of the big toe.



FIG 3A—Case No 6398 At three weeks with tongs in position Shows callus commencing on tibia

No. 11399 had a fracture of the shaft of the lower third of the ulna.

The length of stay in the hospital was prolonged by these other injuries in two cases, both fractured femurs, but was not affected in the other two.

*Treatment.*—Of the thirty-five patients, nineteen were treated by immobilization in posterior and lateral molded plaster splints. In eight patients an anæsthetic was given and a manual reduction done before the application of plaster splints. The fragments slipped in three of these, two of whom had tongs inserted in the malleoli on the fourth and sixteenth days, respectively, and one had a Steinman pin inserted in the os calcis on the ninth day.

One patient was treated in adhesive plaster traction, but not from choice. He had a large wound of the heel which prevented the use of a Steinman pin

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and close enough to the malleoli so that we did not care to insert tongs. He also had a fractured femur on the same side treated by ice tongs.

In two cases tongs were inserted in the malleoli as the primary treatment. In one of these, the tongs were removed on the thirtieth day when union was commencing. In the other they slipped on the sixth day and were reinserted. They slipped again on the forty-first day and adhesive plaster traction was substituted. Tongs were also used in two other cases mentioned above, after immobilization in plaster had been unsuccessful. In one of these the tongs slipped five days after insertion and a Steinman pin through the os calcis was substituted. In the other the tongs slipped six days after insertion and plaster traction was substituted, followed ten days later by Steinman pin

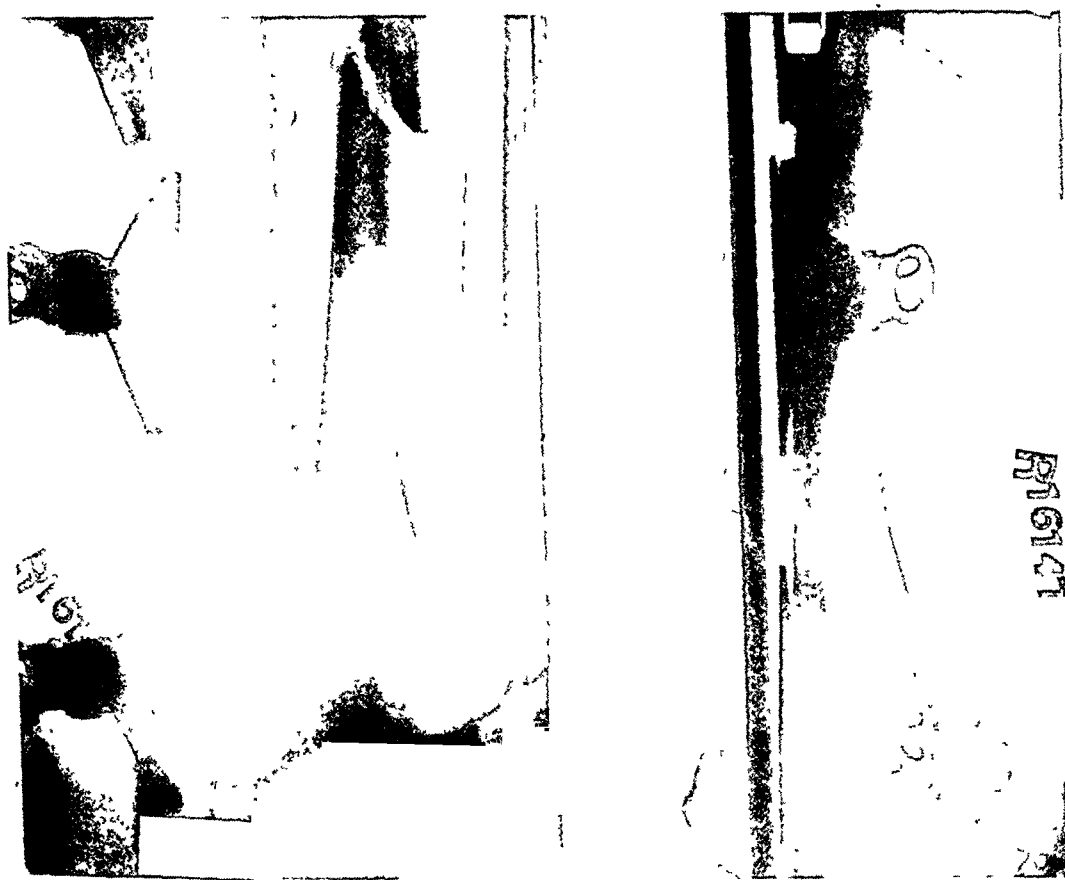


FIG. 3B.—Case No. 6398. At eight weeks in adhesive plaster traction. No overriding, good alignment. Fair callus on tibia.

because of overriding of fragments. In other words, tongs were inserted five times and slipped four times.

Insertion of a Steinman pin through the os calcis was used as the primary treatment in ten cases, after plaster had been unsuccessful in one case and after tongs had slipped in two cases, a total of thirteen patients. Fifteen pounds' traction were usually applied in the primary cases and reduced to ten in from seven to ten days. In the secondary cases the first weight put on varied from twenty to thirty pounds. The Steinman pin remained in for periods from thirty to ninety-four days with an average of fifty-six days. This is longer than is usually advised, but there seems to be little difficulty



in the healing of the wounds produced by the pins and change of position may occur by removing the pin before union is firm, *e.g.*, overriding, dishing, and angulation. On removal of the pin two patients had adhesive plaster traction suspension applied and the remainder plaster splints. Traction suspension was used on three other patients, but they were transferred too early to know the value of the treatment. The position was good on transfer. Of the sixteen patients treated by traction suspension, nine were simple fractures and seven compound. Four patients had an extensive débridement done on admission to the hospital.

*Callus.*—The presence of callus was not mentioned in five cases. It was

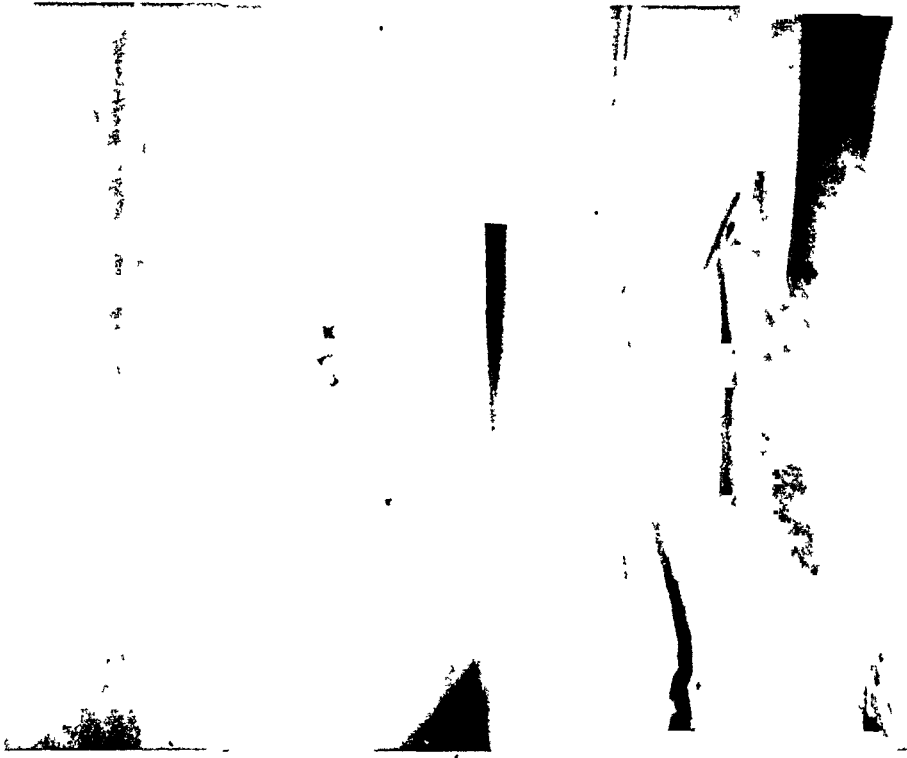


FIG 4—Case No. 10145. Fracture of both bones, middle third. Reduced and plaster splints applied. At six days showed slipping of fragments as above.

noted in the X-ray report for the first time as being present in twenty-four cases at a period varying from sixteen to eighty-six days with an average time of thirty-eight days. Omitting the three children, the average time that the first appearance of callus is mentioned is forty days. Again omitting two cases in which it appeared late, eighty and eighty-six days, the average becomes thirty-six days. The earliest appearance of callus in an adult was twenty-one days. On the last X-ray report while in hospital it is said that *no callus was present in six cases*. These pictures were taken on the thirty-fifth, fifty-sixth, fifty-seventh, eighty-eighth, ninety-fifth and one-hundred-fourteenth days. All obtained solid union except the last two. One of these I have been unable to locate and the other is the patient mentioned later as being still in the Montefiore Hospital at ten months.

*Union.*—The time of bony union is not mentioned in ten cases. In fifteen

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patients it was noted that firm union occurred at periods varying from twenty-five to one hundred nine days with an average of fifty-two days. Solid union is mentioned on sixteen charts as having occurred at periods varying from thirty-eight to two hundred ninety days with an average of ninety-two days. This included cases requiring one hundred, one hundred twenty, one hundred thirty-three, one hundred fifty-four and two hundred ninety days, respectively, so that the average of the remainder was considerably below ninety-two days. The patient whose fracture was solid in thirty-eight days was thirteen years old. It is definitely known that solid union was obtained in all except four patients. Two of these showed satisfactory callus formation

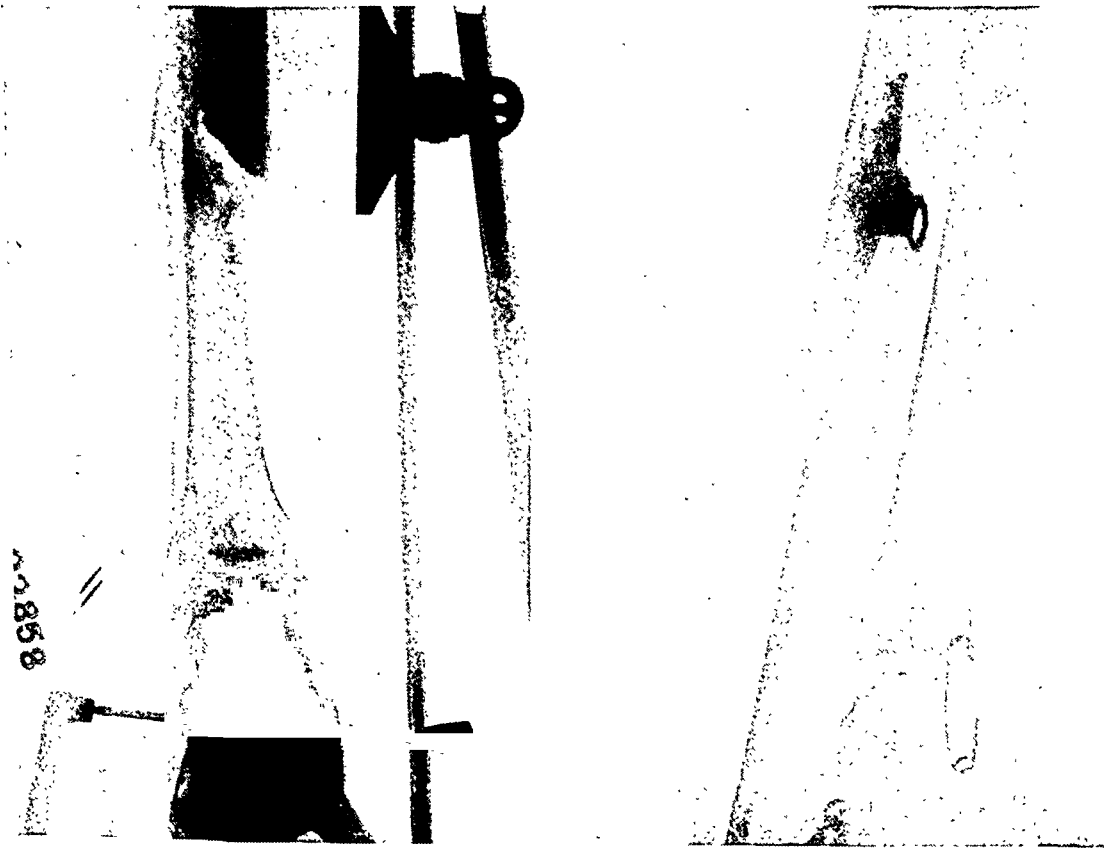


FIG. 4A.—Case No. 10145. Shows good axis and slight overpulling with traction applied by Steinman pin.

when discharged less than thirty days after injury. They could not be traced but with callus appearing in this short time there seems little doubt that they obtained solid union. The third patient, No. 12181, showed no evidence of union at one hundred fourteen days and had a posterior angulation of forty degrees. He had been treated by Steinman pin. He was aged fifty-two and in bad general condition, suffering from generalized arteriosclerosis, auricular fibrillation, *etc.* He was transferred to Montefiore Hospital at four months. At ten months it was reported to me that he was still in the hospital, walking with a cane with the leg in plaster, and that union was progressing slowly. However, I have entered him as non-union. The fourth patient did not have union at the ninety-fifth day. I have been unable to locate him and he may have non-union. This gives at most 6.5 per cent. non-union. The

patient who did not have solid union until two hundred ninety days was a compound fracture with osteomyelitis and sequestration.

The rating of the anatomical result was not possible in three cases as they were transferred to other hospitals before union was obtained. Of the remaining thirty-two patients twenty-four were rated A<sup>2</sup>, seven A<sup>3</sup>, and one has non-union.



FIG. 5.—Case No. 7028. Oblique fracture of both bones with displacement of lower fragments backward. Reduction and plaster splints. Fragments slipped as shown above.

*Deformity in A<sup>3</sup> patients.*—No. 3528.—One-half-inch shortening, compound fracture, treated in plaster splints.

No. 5019.—Apposition 50 per cent. treated in plaster splints.

No. 8156.—One-half-inch shortening, occurring after Steinman pin was removed on thirtieth day and plaster splints applied.

No. 9047.—Angulation with convexity anteriorly and laterally; fragment pierced skin late following necrosis of skin over it and a low-grade osteomyelitis was set up; treated with Steinman pin.

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No. 9098.—Angulation of thirty degrees with convexity outward, treated in adhesive plaster traction because of large loss of tissue at heel; also had ice tongs in femur for fracture of shaft of femur.

No. 11063.—Apposition 50 per cent.; treated by Steinman pin traction; also had ice tongs in femur for fracture of femur same side.

No. 11172.—Apposition 50 per cent., treated in plaster splints.

*Late results.*—The result after one year was obtained in seventeen patients. In fourteen this was  $E^4$ ,  $F^4$ . In two the economic result is not known but functionally they are  $F^3$  and  $F^2$ , respectively. The other patient is still in a hospital with non-union.

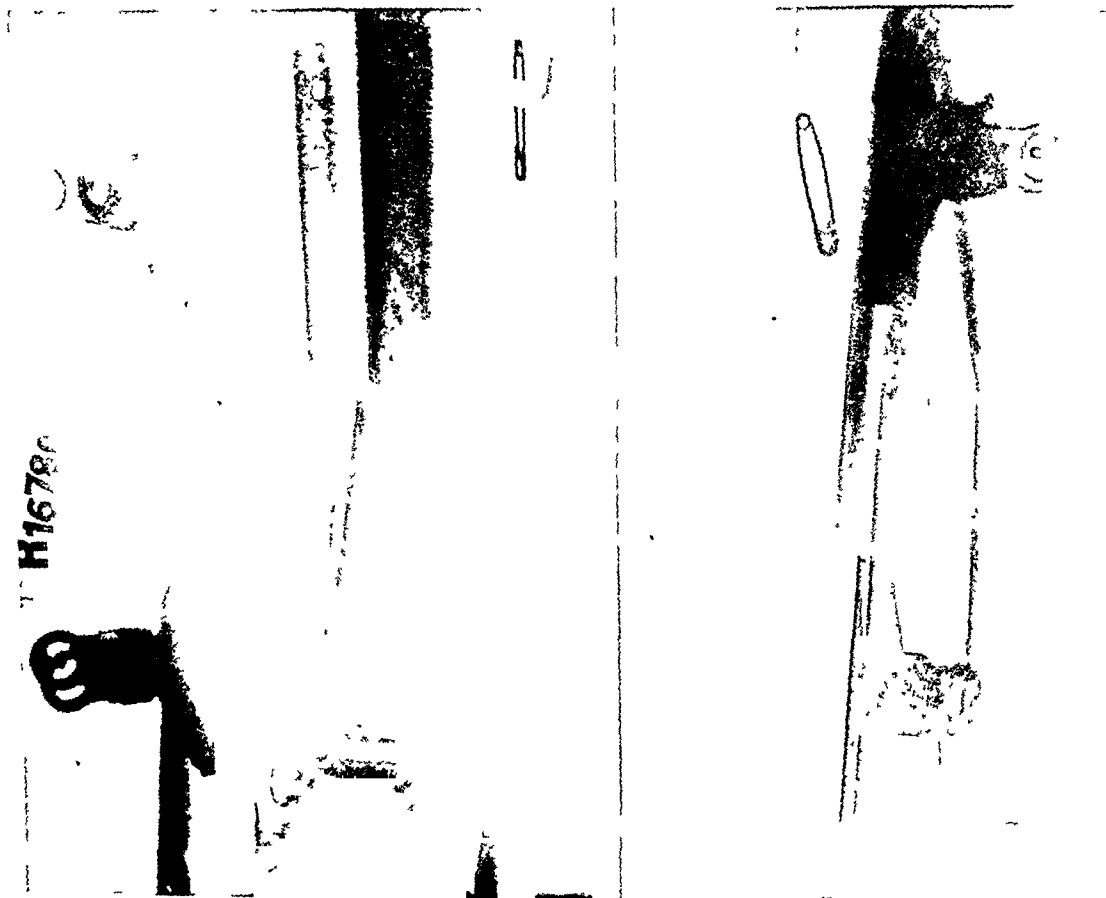


FIG. 5A.—Case No. 7028. Good alignment with traction by Steinman pin.

No. 6207.— $A^4$ ,  $E$  unknown,  $F^3$ .—Compound, comminuted fracture with osteomyelitis. At twenty-two months still complained of pain in ankle and some limitation of dorsiflexion of foot.

No. 9047.— $A^3$ ,  $E$  unknown,  $F^2$ .—Had an infected hæmatoma at site of fracture with subsequent osteomyelitis. Wound remained open for nine months. Treated by Steinman pin and had splints on up to four months. Case settled by Department of Labor at one and one-half years giving him 50 per cent. disability on account of defective motion of both knee and ankle. I doubt if this is permanent.

Of the six other patients with  $A^3$  result, four had  $E^4$ ,  $F^4$  and two could not be traced.

The progress of the patient was complicated in four instances as follows: *Gas bacillus infection*, one. No. 1923.—Severe compound, comminuted

fracture. Débrided, wound left open, and treated by Carrel-Dakin method with leg in plaster splints. Three days later showed definite gas bacillus infection. Leg laid open from two inches below knee to internal malleolus. Given four hundred cubic centimetres of tetanus perfringens serum intravenously in twenty-four hours. Made a good recovery and was up in wheel chair on twenty-ninth day. Result A<sup>4</sup>, E<sup>4</sup>, F<sup>4</sup>.

*Infected hæmatoma, one.*

*Necrosis of skin over bone with later discharge of superficial bone fragments, two.*

There were no amputations and no deaths in this group. There were no open reductions, except manual reduction at the time of débriding compound



FIG. 5B.—Case No. 7028. Position at six weeks. Pin has been removed and plaster splints applied.

fractures. Five patients did not have solid union until after one hundred days and must be considered delayed union, *i.e.*, 14 per cent.

LOWER THIRD.—In this group there were fifty patients of whom forty-four were male and six female. Their ages were as follows: 0 to 15 years, 11; 16 to 29 years, 11; 30 to 39 years, 9; 40 to 49 years, 8; 50 to 59 years, 8; 60 to 69 years, 2; 70 to 79 years, 1. Thirty-nine were simple and eleven were compound fractures. Four were apparently compounded from within and seven from without. Twenty-seven, or over half, were comminuted. Thirty-three were apparently injuries by direct violence. Twenty-two were from automobile accidents. Ten patients had other injuries, but none of these lengthened their stay in the hospital. These were as follows:

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CASE No. 2506.—Fracture of four metatarsals and two toes.

CASE No. 3778.—Fracture of upper third of shaft of humerus.

CASE No. 4605.—Fracture through external condyle of femur.

CASE No. 4672.—Fracture of greater tuberosity of humerus.

CASE No. 6895.—Fracture of base of fifth metatarsal.

CASE No. 8167.—Dislocation of shoulder.

CASE No. 9248.—Fracture of all metatarsals.

CASE No. 9908.—Fracture of internal malleolus.

CASE No. 10897.—Fracture of radius and ulna, middle third.

CASE No. 12593.—Dislocation of foot.

*Treatment.*—Of the fifty patients, thirty-six were treated primarily by immobilization in posterior and lateral molded plaster splints. In fourteen of these an anæsthetic was given and a manual reduction done before the application of splints. In the remainder no anæsthetic was given because only slight or no manipulation was necessary. Two of these reductions were done under the fluoroscope. This primary treatment was unsuccessful in seven patients. Two of these were satisfactorily reduced by a second manipulation under general anæsthesia with application of plaster splints. The remaining five had traction-suspension treatment by means of Steinman pin through the os calcis.

Thirteen patients had a Steinman pin inserted as their primary treatment, *i.e.*, the Steinman pin was used altogether eighteen times. Fifteen pounds' traction were usually employed in the primary cases, later reduced to ten, and twenty to thirty pounds employed in the secondary cases. The Steinman pin broke in one case on the thirty-fourth day and was removed. In another case it was removed before the patient's transfer to Bellevue Hospital on the sixteenth day. One patient died after seventy-two hours and another had an amputation on the twenty-fifth day. In the remaining cases it was left in for periods from twenty-seven to seventy-seven days, with an average of forty-three days. Omitting the probable non-union case mentioned later, in whom the pin was left for seventy-seven days, the average duration of this treatment was forty days. On removing the pin, one patient had adhesive plaster traction suspension for a time and the remainder were placed in plaster splints. Of the eighteen patients treated by traction suspension ten were simple and eight compound fractures.

In all patients the wounds at the site of the Steinman pin healed promptly. In two cases, however, abscesses developed later.

CASE No. 2954.—Wounds healed promptly and never reopened. Four and a half years later he was admitted to the hospital with an abscess on the external aspect of the heel deep to the scar of the pin wound. This was incised and found to lead down to bare, rough bone. It was drained, healed promptly and he has had no further disturbance for the past year.

CASE No. 11894.—The pin broke during treatment and was removed. Wounds healed promptly. Six months later he was readmitted to the hospital on account of persistent pain in the heel. Radiograph showed a small piece of metal lying in the centre of the os calcis surrounded by an abscess two centimetres in diameter. This was opened, metal removed and drained. The wound healed promptly and has given no more trouble for

the past six months. The pin used in this case was of the screw type, which we do not believe is advisable.

One patient had an open reduction on the fifth day with the application of a vanadium steel plate and immobilization in plaster splints. Seven patients

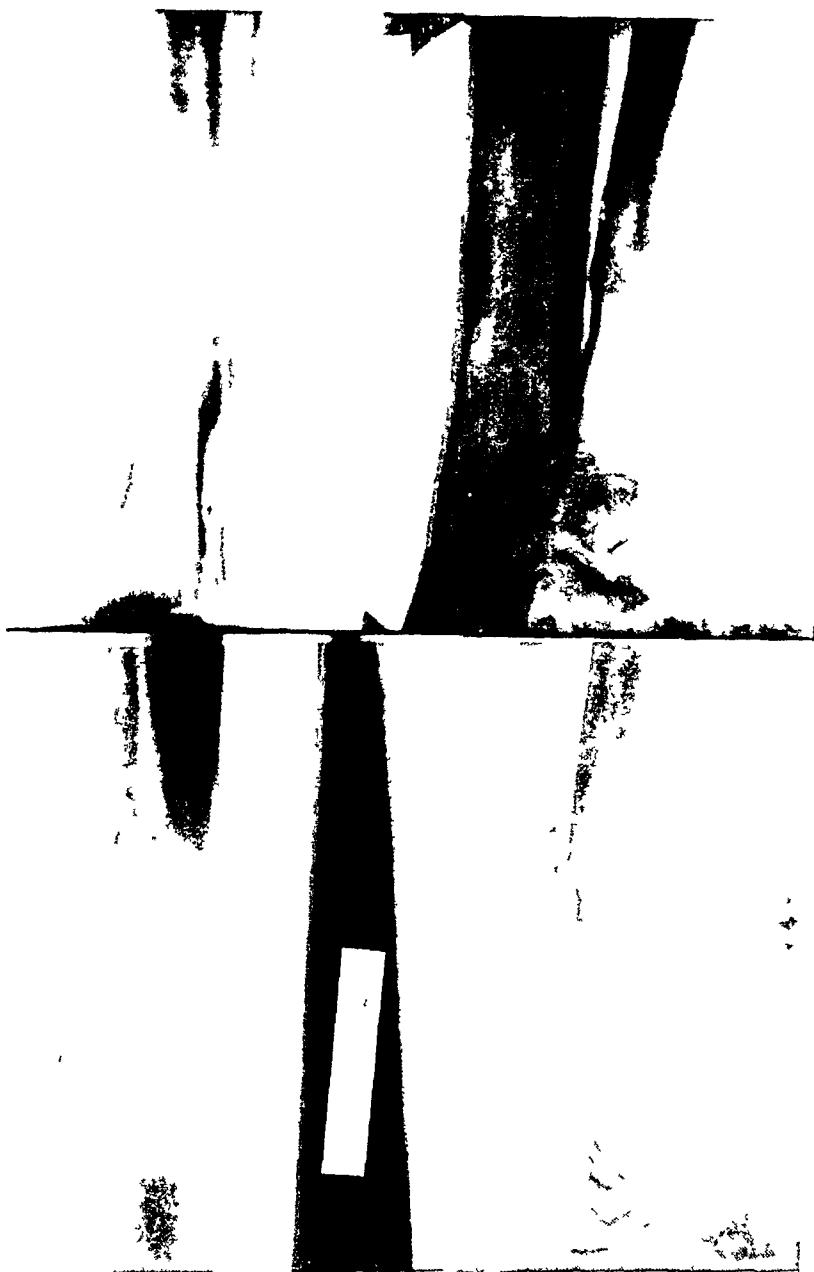


FIG 6—Case No 9908 Comminuted fracture of both bones, lower third. Lower views show position on admission Upper views show position at forty days after traction has been removed and callus has begun to form.

with compound fractures had a débridement done on the day of admission and in five of these a manual reduction was done with the bones visible in the depth of the wound. Of these, splints were applied afterwards in three cases and a Steinman pin used in two.

In three cases the Delbet splint was applied late for weight bearing. It was not used as a primary treatment.

*Callus.*—The first appearance of callus is mentioned in the X-ray report in nine cases at periods varying from twenty to seventy-three days, with an average time of thirty-nine days. Omitting two children of ten and eleven years who showed callus in twenty-eight and thirty days respectively, the average time for noting first appearance of callus was forty-two days. The earliest appearance of callus in an adult was twenty days. On the last X-ray report while in hospital it is mentioned that no callus was present in twelve cases. These pictures were taken on the twenty-seventh, twenty-seventh, thirtieth, thirty-second, thirty-fifth, thirty-sixth, thirty-ninth, forty-third, forty-fifth, forty-seventh, sixty-ninth and ninety-first day. In the first seven



FIG. 6A.—Case No. 9908. Shows position of fragments maintained in traction by Steinman pin. No overriding. Good axis.

one would hardly expect to see callus judging from the average time mentioned above. Of the other five we know that three obtained solid union. The patient who showed no callus at forty-five days I have been unable to locate. The patient who showed no callus at ninety-one days still had a false point of motion at fifteen months. Operation was advised from three months on because of the delay in union but the patient persistently refused. I believe he has periosteum or fascia between a portion of the fragments.

*Union.*—Three patients died, two had amputations and nine could not be traced. In all of these nine, the condition was such when last seen that one would expect good union. Of the remaining thirty-six, it is definitely known that thirty-five obtained solid union, or 97 per cent. The one remaining patient was discussed above under "callus" and had non-union when last seen at fifteen months. As regards the time of union, it is entered on the charts



that eighteen patients showed firm union at periods varying from twenty-eight to seventy-four days, an average of forty-nine days. Solid union is mentioned on seventeen charts as having occurred at periods varying from thirty-two to eighty-six days, with an average of fifty-seven days. The patient showing solid union at thirty-two days was seven years old. A man of twenty-three had solid union at thirty-six days and one of fifty-five at thirty-seven days.

### *Complications.*

#### Deaths, 3.

CASE No. 2718.—Simple fracture of tibia and fibula at junction of middle and lower thirds with forward and inward displacement of lower fragments. Condition satisfactory before anæsthetic, not being in much shock. Heart and lungs negative. Ether anæsthesia lasting twenty minutes. Under fluoroscope the fragments were brought into alignment with slight traction and manipulation. Two lateral molded plaster splints were applied. The patient vomited as he came out of the anæsthetic. He had reacted completely one hour after administration. Three and one-half hours after manipulation he became cyanotic with considerable respiratory distress, slight cough and bloody expectoration. Died two hours later, apparently of pulmonary embolism. Autopsy not obtained.

CASE No. 6954.—Severe compound fracture of both bones of the leg, lower third. Under gas-oxygen-ether anæsthesia wound débrided and Steinman pin inserted in os calcis. Forty-eight hours later developed delirium tremens. At this time also there was suggestion of gas at upper end of wound. Given sixty cubic centimetres of tetanus perfringens serum. Delirium continued and patient died seventy-two hours after injury. We believed his death was due to delirium tremens and not to gas bacillus infection *per se*. No autopsy.

CASE No. 12593.—A man of seventy in poor general condition sustained a simple fracture of both bones of the leg in the lower third, a fracture of the lower extremity of the tibia and a dislocation of the foot. Reduction was attempted without anæsthesia on the first and fourth days, but the fragments slipped each time. On the eighth day a third attempt was made under spinal anæsthesia. The circulation was poor and blebs developed. On the thirteenth day a streptococcus infection of the skin was noted. It was decided that his general condition did not warrant serum therapy. He died on the fifteenth day apparently of sepsis. No autopsy obtained.

#### *Gas bacillus infection, three.*

CASE No. 2954.—Severe compound comminuted fracture of both bones at the junction of the middle and lower third. Débridement, manual reduction, closure of wound. Gas bacillus infection evident within twenty-four hours. Opened widely and given four hundred cubic centimetres of tetanus perfringens serum intravenously in one-hundred-centimetre doses. Had a prolonged but excellent recovery.

CASE No. 6954.—See above under "Death."

CASE No. 9462.—Severe compound fracture of both bones of leg, lower third. Débridement, manual reduction, Steinman pin, wound left open. On the third day showed evidence of gas infection. Leg was opened widely and the patient was given tetanus perfringens serum. Gas infection was controlled within forty-eight hours, but a colon bacillus infection persisted requiring repeated incisions. The process continued to extend and a disarticulation through the knee-joint was done on the twenty-fifth day. Later, after the wound had cleaned up, an amputation was done through the lower thigh and patient made a good recovery.

#### *Amputations, two.*

CASE No. 2506.—A man of sixty-five with markedly sclerotic blood-vessels sustained a simple comminuted fracture of both bones of the leg in the lower third, a fracture

## FRACTURES OF LEG

of four metatarsals and of two toes. He developed many blebs after the first reduction. This was unsatisfactory and a second reduction was attempted at which some of the blebs were broken. He developed many large ulcers of the foot and ankle so that an amputation was done through the middle of the leg on the twenty-second day. He made a good recovery.

CASE No. 9462.—See above under "gas bacillus infection."

*Osteomyelitis*, one.

One patient with a compound fracture developed an abscess with a superficial osteomyelitis, which healed in a brief period spontaneously.

In this series the fractures of the lower third of tibia and fibula presented complications more frequently and of greater severity than in the other groups.

The rating of the anatomical result was not possible in six cases as they were transferred before union was obtained. Three others died and two amputations were performed. Rating was therefore possible in thirty-nine cases. Of these thirty-one were A<sup>4</sup> and eight A<sup>3</sup>.

*Deformity in A<sup>3</sup> patients.*—CASE No. 6130 A<sup>3</sup>.—Fifteen degrees' angulation outward at site of fracture.

CASE No. 6895 A<sup>3</sup>.—Badly comminuted and shows considerable thickening immediately above ankle-joint, axis normal.

CASE No. 7279 A<sup>3</sup>.—Lower fragment of tibia displaced outward and forward, sixteen years of age.

CASE No. 8167 A<sup>3</sup>.—Moderate pronation of foot on weight-bearing.

CASE No. 8816 A<sup>3</sup>.—Fifteen degrees' angulation and one-fourth-inch forward displacement of lower fragment in patient thirteen years of age.

CASE No. 10775 A<sup>3</sup>.—Some visible deformity with slight dishing.

CASE No. 10897 A<sup>3</sup>.—Slight abduction of lower fragments of both bones; slight pronation of foot.

CASE No. 12701 A<sup>3</sup>.—Oblique fracture with one-half-inch shortening.

Four of these A<sup>3</sup> patients were treated by traction and four by plaster splints.

*Late result.*—The result after one year was obtained in eighteen patients. In fifteen this was E<sup>4</sup>, F<sup>4</sup>. In two of the remaining three it was E<sup>4</sup>, F<sup>3</sup> and in the other F<sup>3</sup>, but the economic result is not known as compensation had not been settled and the patient had not returned to work.

CASE No. 6895 A<sup>3</sup>, F<sup>3</sup>.—Has not returned to work at one year. Has about one-half normal range of motion at ankle-joint.

CASE No. 10775 A<sup>3</sup>, E<sup>4</sup>, F<sup>3</sup>.—At one year still complained of discomfort in ankle region and at site of fracture, increased by weight bearing. Had been at usual work several months.

CASE No. 11860 A<sup>4</sup>, E<sup>4</sup>, F<sup>3</sup>.—Moderate loss in mobility at ankle-joint in all directions.

In addition, there is one patient with non-union. Two of the A<sup>3</sup> patients are mentioned above. Two others could not be traced. The remaining four with A<sup>3</sup> result all had E<sup>4</sup>, F<sup>4</sup>.

In addition to the above groups of patients there were seven admitted to the hospital who had fractures of the shaft of both bones of the leg. This injury was only an incident among multiple severe injuries and all died of shock within twenty-four hours. Four were automobile accidents. In all the only treatment instituted was immobilization and the routine for shock. They are not included in the detailed report.

The patients in all these groups have had heat and massage, which are commenced as early as it is practical. If the leg is in splints, the lateral splint is removed by the third or fourth day and this treatment is given daily, unless it is believed that the danger of slipping is too great. Active motion at the ankle-joint is encouraged early. If a simple fracture is in traction, heat and massage are begun about the same time as in plaster. In compound fractures the time depends on the condition of the wound. Passive motion is reserved until such time as union is fairly firm, believing that otherwise the operator may do damage. However, much can be accomplished by getting the early coöperation of the patient in active motion. Eleven of the earlier patients in this group received diathermy. It was stopped because not only did we fail to find it of value, but in several cases we felt definitely that callus was absorbed during its use and the time of healing prolonged.

In these patients we have used various chemical aids in treatment, *viz.*, calcium chloride, calcium with phosphates, thyroid extract, parathyroid extract, irradiated ergosterol and cod-liver oil. This has been done from the day of admission on series of cases and it has also been used on definitely delayed cases. We have no evidence that any one of these is of the slightest value, either in normal or delayed healing. We still use cod-liver oil in most of these cases, believing that there may be some nutritious effect for the patient confined to bed for a prolonged period. All the other chemical aids have been discarded.

## SUMMARY

1. This is an analysis of 107 patients with fractures of both bones of the leg, not involving the joints, of the following types: (a) Spiral, thirteen; (b) upper third, nine; (c) middle third, thirty-five; (d) lower third, fifty.

2. The age grouping was as follows: 0 to 15 years, fifteen; 16 to 29 years, twenty-seven; 30 to 39 years, twenty-two; 40 to 49 years, twenty; 50 to 59 years, seventeen; 60 to 69 years, five; 70 to 79 years, one. About two-thirds of the patients were between the ages of sixteen and fifty.

3. There were ninety-seven males and ten females.

4. Sixty-two fractures appear to have been sustained by direct and forty-five by indirect violence. Thirty-nine patients were injured in automobile accidents.

5. Eighty were simple and twenty-seven compound fractures. Sixty were comminuted fractures.

*Treatment.*—*Primary.*—Plaster-of-paris splints, seventy; traction by Steinman pin through os calcis, thirty; traction by ice tongs, four; traction by adhesive plaster, two; open operation (Lane plate), one.

The position of the fragments in plaster was unsatisfactory eleven times and in two cases treated by ice tongs, which slipped.

*Secondary, i.e., primary was unsatisfactory, fourteen*—Traction by Steinman pin, seven; traction by ice tongs, four (one reinserted); traction by adhesive plaster, one; open operation (Lane plate), one; open operation for interposition (kangaroo-tendon sutures), one.

The ice tongs slipped in three of these cases. The Steinman pin was substituted in two and adhesive plaster in one.

Traction suspension was used in some form on forty-six patients. The Steinman pin was used during treatment thirty-nine times. Ice tongs were used eight times and were unsuccessful five times. Open operation with Lane plating was done twice, and with kangaroo-tendon sutures once.

When the treatment was completed, the average time for retaining the Steinman pin or ice tongs was forty-eight days. All pin and tong wounds healed promptly, but there were two late abscesses.

7. Of the entire series, callus was first noted in the X-ray in forty cases as appearing in an average time of forty days. The average period before solid union was obtained was: Spiral, eighty-four days; upper third, ninety-five days; middle third, ninety-two days; lower third, fifty-seven days.

Among the twenty-seven compound fractures there were five gas bacillus infections. All had wide incisions and tetanus perfringens serum. Three made excellent recoveries. In one patient the gas bacillus infection was readily controlled but he had a late amputation because of continual pocketing and spreading of pus, apparently chiefly of the colon group. One died on the third day, apparently of delirium tremens.

9. *Results*.—Death, three; amputation, three; cases transferred to other institutions too early to be certain of result—position in all such as to expect solid union, eleven; cases discharged from hospital too early for union to be solid, and could not be traced—no reason to expect delayed union in any, five; known solid union, eighty-two; known non-union, two; probable non-union, which cannot be traced, one.

10. Those patients on whom hospital treatment was completed actually remained in the hospital for an average period of sixty-six days.

11. *Rating*.—Forty-two were rated according to the Massachusetts General Hospital rating after one year as follows:  $A^4$ ,  $E^4$ ,  $F^4$ , twenty-five;  $A^4$ ,  $E^4$ ,  $F^3$ , one;  $A^4$ ,  $E^0$ ,  $F^4$ , two;  $A^4$ ,  $E^0$ ,  $F^3$ , one;  $A^3$ ,  $E^4$ ,  $F^4$ , nine;  $A^3$ ,  $E^4$ ,  $F^3$ , one;  $A^3$ ,  $E^0$ ,  $F^3$ , one;  $A^3$ ,  $E^0$ ,  $F^2$ , one;  $A^2$ ,  $E^0$ ,  $F^3$ , one.

The  $E^0$  cases were those whose compensation had not been settled when last heard of and had not attempted to return to work.

In addition there were thirty-six patients with an  $A^4$  result and four with an  $A^3$  result whose economic and functional results are not known.

Averaging the time before returning to work in New York City does not give a correct picture of the duration of disability. Most of these patients are covered by the compensation laws and do not return to work until their cases have been settled. For various reasons this is often delayed long after a man is fit for work. Particularly is this true because there is no arrangement for part time or light duty, but a man must return to full time on his old job or be given a per cent. of permanent disability. This permanent disability frequently improves rapidly after compensation is settled.

We cannot insist too strongly that fractures deserve thorough treatment and that better results can be obtained on services where special interest is

shown in them. There is no single method applicable to all types in all places. We have presented one group of fractures in which the more complicated cases have been treated largely by methods of traction suspension. We do not believe this method is any easier or requires any less training than open reduction. We do believe that traction is less dangerous to the patient than an open operation if he is to be treated by a surgeon who only occasionally sees a major fracture.

Further, traction is important as a method of treatment because it gets us into the habit of expecting bones to unite without overriding and in the proper axis. Union is a most necessary factor, but the number of cases of malunion can be considerably diminished by the proper application of the methods of traction. Several clinics believe in early weight bearing and have their patients return to industry wearing splints. We cannot do that usually in New York as a man does not return to industry until his compensation case is closed. We believe in early motion and late weight bearing, *i.e.*, after union is solid.

Theoretically, traction exerted on the lower end of the tibia is preferable to that brought through the ankle-joint. Practically, we have not been satisfied with ice tongs in the malleoli and have given this up in favor of the Steinman pin through the os calcis. We have not seen loss of function nor instability of the ankle-joint which we felt could in any way be attributed to the prolonged pull through the ligaments of the ankle-joint.

For the type of patient we have in the district where we work, we believe that in fractures of the shaft of both bones of the leg, traction suspension in complicated cases offers the best chance of a good result in a reasonable time.

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# THE COMPARATIVE VALUE OF METAPHEN IN ALCOHOL- ACETONE-AQUEOUS SOLUTIONS IN THE PRE-OPER- ATIVE DISINFECTION OF THE SKIN

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PERHAPS in no branch of surgical technic has there been a greater diversity of opinion than in that of pre-operative skin disinfection. The existence of this difference of opinion has been indicated by the colorful array of pre-operative skin disinfectants in daily use in the larger surgical clinics throughout this country. The reason behind this confusion has been that up to the present moment no chemical nor combination of chemicals has possessed the varied and exacting properties required of the ideal pre-operative skin disinfectant.

In addition to possessing high bactericidal action as well as deep penetrability, the ideal skin disinfectant must meet certain other definite requirements before it is worthy of consideration in pre-operative skin sterilization. It must not cause pain at the time of application, nor dermatitis subsequently. The method of application must be simple and the drying time should be so regulated that sterilization and penetration can be accomplished with a minimum loss of time. It must be capable of dissolving the skin debris, consisting of glandular secretions and excretions, degenerative cellular products, and dirt in which bacteria are so frequently found. Within the microscopic crevices of the skin are very tiny air bubbles which must be decomposed and removed by the disinfecting solution before satisfactory penetration and sterilization can be accomplished. As a protection against any retardation of the process of wound healing following its use, the preparation must be of relatively low toxicity to normal tissue and also should not precipitate in the presence of blood serum. Lastly, the ideal skin disinfectant should have a sufficiently high color in order to remove any doubt concerning the extent of the field prepared for operation.

Although the iodine-alcohol technic of skin disinfection fails in many respects to meet the requirements mentioned above, it has been in more or less general use since its introduction by Grossich<sup>1</sup> in 1908. It has been well known that some individuals, especially those suffering from hyperthyroidism, have a marked idiosyncrasy to iodine, and that in these cases annoying skin irritation has sometimes resulted from its use. The drug also has tended to concentrate along the margins of the field and unless special care was exercised in removing these marginal accumulations, skin burns occurred. The removal of the iodine with alcohol before the patient was draped and the skin incision was made possessed two objectionable features. In the first place, such a method was quite time-consuming, and, secondly, the

extent of the field prepared for operation was ill-defined following the removal of the compound. It has been claimed by some investigators, among these O'Connor<sup>2</sup> and Maylard,<sup>3</sup> that iodine used in the peritoneal cavity results in the development of severe post-operative adhesions. When tincture of iodine was mixed with blood serum, precipitation always occurred with subsequent loss of bactericidal power.

The 5 per cent. alcoholic solution of picric acid has not been generally accepted as a pre-operative skin disinfectant for a number of reasons. Occasionally, severe skin irritation has occurred following its use. The tendency to crystallize and the slow drying time have also been objectionable features. The picric acid solution not only stained the operating-room sheets and towels at the time of operation, but also discolored the patient's clothing, bedding, *etc.*, for a period of several days following its use. Furthermore, linen that had been saturated with picric acid solution and then allowed to dry was inflammable, a fact that had always to be remembered when the use of the cautery or diathermy was contemplated.

Neutral acriflavine has not lent itself to pre-operative skin disinfection for a number of reasons. As shown by Browning and colleagues,<sup>4</sup> Graham-Smith,<sup>5</sup> and others, this compound possessed a very slow killing rate and a high inhibitory power. Dakin and Dunham<sup>6</sup> have shown that a 1 to 1000 dilution of acriflavine required more than six hours to kill staphylococcus aureus in blood serum, muscle extract, or in defibrinated blood. Young and his co-workers<sup>7</sup> have shown that a solution of 1 to 200 of neutral acriflavine suspended in 50 per cent. dog serum failed to kill bacillus coli in one hour. A 5 per cent. solution of neutral acriflavine dissolved in 50 per cent. alcohol and 10 per cent. acetone, as advocated by Tinker and Sutton,<sup>8</sup> had to be used in fresh preparations if its maximum efficiency as a skin disinfectant was desired. The lack of stability plus its relatively high cost have tended to decrease its popularity as a pre-operative skin disinfectant even if in other respects it had met the requirements of the ideal preparation.

Because of its tendency to cause smarting and burning of the skin at the time of its application, "Kalmerid," a 1 per cent. solution of potassium mercuric iodide in 80 per cent. acetone, has decreased in its popularity with the increasing use of local anæsthesia in surgery. Cases of marked dermatitis have occasionally been observed in urology following the use of "Kalmerid" on the external genitalia. Furthermore, when this solution was mixed with blood serum, precipitation occurred rapidly, resulting in a marked loss of bactericidal power.

The search for a pre-operative skin disinfectant which could be used upon the delicate epidermis of the external genitalia without fear of discomfort at the time of application or subsequent dermatitis, resulted in the introduction of an alcohol-acetone-aqueous solution of mercurochrome by Scott and Hill.<sup>9</sup> This preparation was made by dissolving two grams of crystalline mercurochrome in thirty-five cubic centimetres of distilled water, and then adding, while stirring, fifty-five cubic centimetres of 95 per cent. alcohol and

ten cubic centimetres of acetone. The persistence of the stain in the operating room, on linen, clothing, *etc.*, has been the most common objection to the use of this preparation.

Realizing that any further progress in the development of the ideal skin disinfectant depended upon the introduction of a chemical possessing more nearly the bactericidal and other properties required of such a preparation, we were finally apprised of the literature on metaphen. Provided the claims made for this germicide could be substantiated, it seemed to us that metaphen would be very suitable for our purposes. At first we experimented with the 1 to 500 alkaline-aqueous solution of metaphen and shortly concluded that it possessed no value in skin sterilization. Because of its enormous antiseptic powers against the commonly encountered microorganisms when tested against these *in vitro*, we were led to believe that the compound might become useful as a pre-operative skin disinfectant if we were able to obtain the crystalline form for the preparation of higher concentrations in alcohol and acetone. More than a year ago, therefore, we informed Doctor Raiziss, of the Dermatological Research Laboratories, of our hopes and requested his coöperation. He very generously sent us twenty grams of the crystalline compound. It seemed essential at first to evaluate the disinfectant and antiseptic properties of metaphen *in vitro* in comparison with other commonly used chemicals before we attempted a study of its disinfecting capacity on the skin.

This preparatory study, by one of us,<sup>10</sup> necessitated an extensive investigation of the disinfecting and antiseptic potency of bichloride of mercury, hexylresorcinol, the aqueous and alcohol-acetone solutions of mercurochrome, tincture of iodine and phenol, against staphylococcus aureus, streptococcus hæmolyticus, gonococcus, bacillus anthracis, bacillus coli and bacillus subtilis. These studies showed that *in vitro* metaphen possessed unusual disinfecting and antiseptic powers far in excess of bichloride of mercury, hexylresorcinol, mercurochrome, tincture of iodine and phenol. It was also demonstrated that metaphen had a low toxicity when injected intravenously in rabbits and that it failed to precipitate out serum proteins in dilutions as low as 1 to 200 and that it exerted no deleterious effect on surgical instruments or rubber. Because of these superior qualities we proceeded with our study of metaphen as a pre-operative skin disinfectant.

During this study, the article of Raiziss, Severac and Moetsch<sup>11</sup> appeared on metaphen as a skin disinfectant. The demerits of this study have been adequately discussed by Leonard<sup>12</sup> and White and Hill.<sup>13</sup> Unfortunately, the latter authors failed to carry the concentration of metaphen higher than a 1 to 500 dilution and erroneously concluded that the compound was unsuitable as a skin disinfectant.

Following a large series of discouraging results with various higher dilutions of both the aqueous and the alcohol-acetone-aqueous solutions of metaphen, we finally arrived at a formula which fulfilled our requirements. It has, of course, been commonplace knowledge that the efficiency of a disinfectant *in vitro* tests has been a far cry from that actually observed in carefully



conducted and controlled *in vivo* experiments. It was, therefore, no particular surprise to us to discover that, although the phenol coefficient of metaphen was 1,500 for staphylococcus aureus and 250 for bacillus coli when studied in the test tube, we were compelled to come down to an alcohol-acetone-aqueous solution of metaphen containing 0.5 per cent. (1 to 200 dilution) of the compound before it exercised its optimum efficiency as a pre-operative skin disinfectant. Since the 7 per cent. solution of tincture of iodine and the alcohol-acetone-aqueous 2 per cent. solution of mercuriochrome have been disinfectants of choice in leading surgical clinics today, the following comparative study was made with these two pre-operative skin disinfectants together with the alcohol-acetone-aqueous 0.5 per cent. solution of metaphen and a control solution containing the alcohol-acetone-aqueous base for both mercurial compounds employed. With these disinfectants, the first part of our study was performed on infected rabbit's skin and the last part on the unwashed human skin.

## EXPERIMENTAL

*Microorganisms employed.*—The study of disinfection on the rabbit's skin was performed with the following organisms commonly encountered in clinical conditions; *viz.*, staphylococcus aureus, streptococcus hæmolyticus, bacillus coli and the spore-bearing organism, bacillus subtilis. The strains of these microorganisms were the same as those made use of in our previous *in vitro* study.<sup>10</sup> The ease with which these microorganisms were recognizable morphologically and culturally rendered them particularly useful in tracing the results of incomplete disinfection back to the original strain employed in the study. The presence of spores in bacillus subtilis was daily ascertained by staining these organisms by Dorner's method with carbol fuchsin and a saturated solution of aqueous nigrosine.

*Chemicals employed.*—(1) *Metaphen.*—The alcohol-acetone-aqueous 0.5\* per cent. solution of metaphen was prepared by dissolving 0.5 gram of crystalline metaphen (4, nitro-5-hydroxy-mercuri-ortho cresol,  $C_2H_2:CH_3ONO_2$ . Hg.) in a mixture of 50 cubic centimetres of 95 per cent. alcohol and 10 cubic centimetres acetone. To the completely dissolved mercurial compound was added slowly, and while stirring, a mixture containing 39 cubic centimetres of distilled water and 1 cubic centimetre of a 1 per cent. aqueous solution of eosin. This pinkish, opalescent solution remained stable in cork-stoppered amber-colored bottles for about four weeks when the mercurial compound slowly began to settle on the bottom. The drying period on rabbit and human skin was about three minutes. No discomfort was experienced on the intact skin of the abdomen, perineum and genitalia. The coloring was delicately pink and the painted area was quite visible. Because of its low surface tension the solution was easily and evenly spread over the skin surface. Linen and clothing soaked in the metaphen solution were readily cleaned with ordinary soap and water. This solution remained harmless to

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\* See Addendum on page 596.

metallic instruments and rubber. When 0.7 cubic centimetres of the solution was mixed thoroughly with 1 cubic centimetre of human serum, precipitation did not occur. The precipitation which did occur at higher concentration was due to the lack of solubility of the mercurial compound in water, rather than to a combination between the constituents of the blood serum and the mercury. Repeated local applications on the skin failed to produce destruction of the surface epithelium.

(2) *Tincture of iodine*.—The 7 per cent. tincture of iodine alcoholic solution was prepared according to the U.S.P. formula, 100 cubic centimetres containing 7 grams iodine and 5 grams potassium iodide dissolved in 1 cubic centimetre of distilled water and mixed with 95 per cent. alcohol.

(3) *Alcohol-acetone-aqueous 2 per cent. mercurochrome*.—This was prepared according to the formula by Scott and Hill<sup>9</sup> and described previously.

(4) *Alcohol-acetone-aqueous solution*.—This control solution was prepared by mixing 50 cubic centimetres of 95 per cent. alcohol, 10 cubic centimetres acetone, 39 cubic centimetres distilled water and 1 cubic centimetre of a 1 per cent. aqueous solution of eosin (the solvent for mercurochrome and metaphen).

*Technical procedure in rabbit-skin disinfection*.—The normal and adult rabbit was strapped down on the dog operating table. The abdomen was completely depilated by applying to the moistened hair a semi-liquid mixture containing one part of barium sulphide and two parts of flour. After depilation was completed, care was taken to remove the chemical thoroughly by allowing lukewarm water to run over the skin. Usually an area measuring fifteen by twenty-five centimetres was prepared and this was subsequently marked off by a red wax pencil into sixty small squares, each measuring about twenty-five square millimetres. The centre of each square was heavily infected with an undiluted eighteen-hour broth culture of one of the strains of microorganisms employed, and allowed to dry. The actual position of the culture was readily visible upon drying owing to its glistening surface. To each area the disinfectant solution was applied by means of an absorbent cotton swab. A contact of exactly three minutes was allowed between the application of the disinfectant and the removal of the culture from the centre of the treated area. The culture was obtained by the following technic: Two wooden applicator cotton swabs (165 by 2 millimetres), previously sterilized in cotton-plugged test tubes (125 by 15 millimetres) for one hour at 156° C., were slightly moistened at their extreme tips in 1 cubic centimetre of sterile broth. The swabs were vigorously rubbed against the centre of the treated area and then with a twirling motion of the fingers the culture was removed. Under strict aseptic conditions the swabs were immediately immersed in 100 cubic centimetres of Douglas' broth contained in a 250 cubic centimetre Erlenmeyer flask. After incubation for forty-eight hours at 37° C., the results of skin sterilization were read. This technic was observed with all the disinfectants employed. The areas not treated with any disinfectant served for control purposes. During the course of this study we were con-

stantly watching for the occurrence of self-disinfection of the skin as recorded by Arnold and his co-workers,<sup>14</sup> a phenomenon not observed by us on the infected rabbit's skin or the unwashed human skin of the upper and inner surfaces of the thigh. Our control material always showed bacterial growth after forty-eight hours' incubation at 37° C., in either Douglas' broth or the ordinary meat extract broth (pH. 7.6). We were also anxious to guard against the transfer to the culture flasks of sufficient disinfectant on the moistened cotton swab, which, in itself, would produce sterilization. With this in mind we inoculated every flask found to be sterile after incubation with one drop of an eighteen-hour broth culture of the strain of bacterium employed in the original test. Subsequent growth following the usual incubation indicated that the original sterility was due to complete skin sterilization of the infected skin area. Furthermore, we endeavored to put each micro-organism and disinfectant to approximately identical experimental conditions by subjecting only one type of organism to the action of all the disinfectants studied, including the controls, on one and the same animal during the same hour of experimentation. When bacterial growth occurred in any one flask after forty-eight hours' incubation at 37° C., smears and cultures were made in order to ascertain that the test organisms were recoverable from the contaminated broth. Having fulfilled all these rigid control tests, the following results were obtained:

*I.—Skin surface disinfection with tincture of iodine, the alcohol-acetone-aqueous solutions of 2 per cent. mercurochrome and 0.5 per cent. metaphen after three minutes' contact with the infected rabbit's skin.*

One hundred separate skin-surface tests were performed with each of the four disinfectants under discussion for the evaluation of their sterilizing capacity against staphylococcus aureus, streptococcus hæmolyticus, bacillus coli and bacillus subtilis, respectively. The results of skin disinfection are shown

TABLE I

*Surface skin disinfection with tincture of iodine, alcohol-acetone solutions of mercurochrome and metaphen after three minutes' contact with infected rabbit's skin*

| Microorganisms                                      | Number of tests with each disinfectant | Number of sterile tests with        |   |  |                      |          |
|---|--|-------------------------------------|---|--|----------------------|----------|
|   |  | Tincture of iodine 7 per cent. sol. | Mercurochrome (2 per cent.) in alcohol-acetone sol. | Metaphen (0.5 per cent.) in alcohol-acetone sol. | Alcohol-acetone sol. | Controls |
| Staphylococcus aureus.....                          | 100                                    | 90                                  | 38  | 88   | 0                    | 0        |
| Streptococcus hæmolyticus.....                      | 100                                    | 76                                  | 57  | 93   | 0                    | 0        |
| Bacillus coli.....                                  | 100                                    | 82                                  | 70  | 87   | 0                    | 0        |
| Bacillus subtilis (spore).....                      | 100                                    | 71                                  | 41  | 91   | 0                    | 0        |
| Percentage of complete sterilization (Average)..... |  | 79.7                                | 51.5  | 89.7   | 0                    | 0        |

# DISINFECTANT VALUE OF METAPHEN

in Table I. The mercurochrome solution produced 51.5 per cent. of complete skin-surface disinfection against all the microorganisms tested; the tincture of iodine produced 79.7 per cent. complete disinfection; and the metaphen solution yielded 89.7 per cent. sterile results. All the skin areas treated with the control alcohol-acetone-aqueous solution, as well as those untreated and used for controls, showed bacterial growth.

II.—*Deep skin disinfection with tincture of iodine, the alcohol—acetone-aqueous solutions of 2 per cent. mercurochrome and 0.5 per cent. metaphen after three minutes' contact with the infected rabbit's skin (pinch grafts).*

For the evaluation of the ability of the disinfectant to penetrate deeply into the infected rabbit's skin, the technical procedure remained the same as that outlined above, except that instead of making surface swab cultures of the centre of the treated areas, small pinch grafts were removed from this region after the microorganisms had been exposed for three minutes to the action of the disinfectant. The scalpel and forceps employed in this study were sterilized in the dry oven for one hour at 156° C. The pinch grafts which were removed measured about three by three by two millimetres. These were immediately transferred to the flasks containing one hundred cubic centimetres of meat extract broth by means of sterile wooden applicator swabs. Twenty-five pinch grafts were removed from the areas treated with the four disinfectants under discussion and with the respective strains of bacteria. The same number of controls was removed from skin areas not treated by any disinfectants. The results of deep skin disinfection are shown in Table II.

In this crucial test of penetrability, we made the interesting and striking observation that neither mercurochrome nor tincture of iodine killed the spore-bearing bacillus subtilis, while metaphen effected 88 per cent. complete

TABLE II

*Deep skin disinfection with tincture of iodine, alcohol-acetone solutions of mercurochrome and metaphen after three minutes' contact with infected rabbit's skin (pinch-graft study)*

| Microorganisms                                      | Number of tests with each disinfectant | Number of sterile tests with        |   |  |                      |          |
|---|--|-------------------------------------|---|--|----------------------|----------|
|   |  | Tincture of iodine 7 per cent. sol. | Mercurochrome (2 per cent.) in alcohol-acetone sol. | Metaphen (0.5 per cent.) in alcohol-acetone sol. | Alcohol-acetone sol. | Controls |
| Staphylococcus aureus.....                          | 25                                     | 14                                  | 2   | 21   | 0                    | 0        |
| Streptococcus hæmolyticus.....                      | 25                                     | 18                                  | 14  | 25   | 0                    | 0        |
| Bacillus coli.....                                  | 25                                     | 14                                  | 10  | 19   | 0                    | 0        |
| Bacillus subtilis (spore).....                      | 25                                     | 1                                   | 0   | 22   | 0                    | 0        |
| Percentage of complete sterilization (Average)..... |  | 47                                  | 26  | 87   | 0                    | 0        |

deep skin disinfection against this hardy organism. Aside from this spectacular capacity of metaphen, the total percentage of complete deep skin disinfection against all the four test microorganisms was 26 per cent. with the mercurochrome solution, 47 per cent. with the tincture of iodine solution and 87 per cent. with the metaphen solution. The control alcohol-acetone-aqueous solution failed to produce any deep skin disinfection while all the control pinch grafts showed growth of the respective microorganisms employed in addition to the normal bacterial flora of rabbit's skin. By inoculating all sterile flasks with one drop of an eighteen-hour broth culture of the strain of bacterium used originally, subsequent bacterial growth took place which indicated that the original sterility was not due to the transfer of enough chemical to induce antiseptis.

III.—*Surface-skin disinfection of unwashed human skin with tincture of iodine, the alcohol-acetone-aqueous solutions of 2 per cent. mercurochrome and 0.5 per cent. metaphen after three minutes' contact.*

Six adult and convalescent surgical patients volunteered their coöperation in these studies. The constancy of bacterial contamination of the upper and inner surfaces of the thigh renders these areas suitable for skin disinfection experiments. The individual tests were so arranged that the identical number of studies was made simultaneously on one and the same person with all the disinfectants under consideration. The technical procedure remained the same as that described on the rabbit's skin, except that the unwashed human skin was not purposely infected with bacterial cultures. The results of surface-skin disinfection are shown in Table III. Fifty-two separate skin surface tests were made with each disinfectant respectively. In 28.8 per cent. of the tests, complete surface-skin disinfection was obtained with the mercurochrome solution, in 96.1 per cent. with the tincture of iodine solution and in 98.0 per cent. with the metaphen solution. Only one in fifty-two tests of attempted skin disinfection with the control alcohol-acetone-aqueous solution was found to be sterile. The untreated areas showed bacterial growth

TABLE III

*Surface skin disinfection with tincture of iodine, alcohol-acetone solution of mercurochrome and metaphen after three minutes' contact with unwashed human skin*

| Number of persons' skin tested                      | Number of tests with each disinfectant | Number of sterile tests with        |   |  |                      |          |
|---|--|-------------------------------------|---|--|----------------------|----------|
|   |  | Tincture of iodine 7 per cent. sol. | Mercurochrome (2 per cent.) in alcohol-acetone sol. | Metaphen (0.5 per cent.) in alcohol-acetone sol. | Alcohol-acetone sol. | Controls |
| 6   | 52                                     | 50                                  | 15  | 51   | 1                    | 0        |
| Percentage of complete sterilization (Average)..... |  | 96.1                                | 28.8  | 98.0   | 3.8                  | 0        |

## DISINFECTANT VALUE OF METAPHEN

in every instance. Control tests showed that the sterile results obtained were not due to the transfer of sufficient amount of disinfectant to induce antisepsis.

IV.—*Deep skin disinfection of human unwashed skin with tincture of iodine, the alcohol-acetone-aqueous solutions of 2 per cent. mercurochrome and 0.5 per cent. metaphen after three minutes' contact (skin-scraping tests).*

These tests were performed for the determination of the ability of the disinfectants under discussion to exercise deep skin sterilization. The unwashed skin on the upper and inner surfaces of the thigh was painted with the respective disinfectants including the control alcohol-acetone-aqueous solution. After the three-minute period of contact, the centres of the skin areas were scraped with scalpels sterilized in the dry oven for one hour at 156° C. The scraping proceeded until capillary bleeding occurred. The scrapings adhering to the knife-blade were removed under aseptic conditions by moistened wooden applicator swabs and were immediately suspended in 100 cubic centimetres of beef extract broth in 250 cubic centimetre Erlenmeyer flasks. The same technical procedure was followed in removing scrapings from the untreated control areas. The results obtained after forty-eight hours' incubation at 37° C. are listed in Table IV. Fifty-two separate skin-scraping tests were performed with each disinfectant respectively. Only two in fifty-two tests, or 3.8 per cent. complete deep skin disinfection was produced by the mercurochrome solution. Forty-four in fifty-two tests, or 84.6 per cent. of complete deep skin disinfection was obtained with the tincture of iodine solution, while forty-nine in fifty-two tests, or 94.2 per cent. of complete deep skin sterilization was produced by the metaphen solution. All the areas treated with the control alcohol-acetone-aqueous solution as well as those untreated showed bacterial growth. Our precautionary study of all sterile flasks proved that antisepsis was not due to direct transfer of disinfectant.

TABLE IV

*Deep skin disinfection with tincture of iodine, alcohol-acetone solutions of mercurochrome and metaphen after three minutes' contact with unwashed human skin (skin-scraping study)*

| Number of persons' skin tested                      | Number of tests with each disinfectant | Number of sterile tests with        |   |  |                      |          |
|---|--|-------------------------------------|---|--|----------------------|----------|
|   |  | Tincture of iodine 7 per cent. sol. | Mercurochrome (2 per cent.) in alcohol-acetone sol. | Metaphen (0.5 per cent.) in alcohol-acetone sol. | Alcohol-acetone sol. | Controls |
| 6   | 52                                     | 44                                  | 2   | 49   | 0                    | 0        |
| Percentage of complete sterilization (Average)..... |  | 84.6                                | 3.8   | 94.2   | 0                    | 0        |

## SUMMARY

1. Surface skin disinfection with the 7 per cent. tincture of iodine, the alcohol-acetone-aqueous 2 per cent. solution of mercurochrome and the alcohol-acetone-aqueous 0.5 per cent. solution of metaphen, after three minutes' contact with infected rabbit's skin, has shown that the undiluted eighteen-hour culture of staphylococcus aureus, streptococcus hæmolyticus, bacillus coli and the spore-bearing bacillus subtilis were killed in 51.5 per cent. of tests with mercurochrome, 79.7 per cent. with tincture of iodine and 89.7 per cent. with the metaphen solution.

2. Deep skin sterilization (pinch grafts) of the infected rabbit's skin with the respective disinfectants and the stated microorganisms has shown that the mercurochrome and tincture of iodine solutions failed to kill the spore-bearing bacillus subtilis after three minutes' contact, while the metaphen solution produced 88 per cent. complete deep skin disinfection against this organism. The total deep skin disinfection against all the respective microorganisms was 26 per cent. with mercurochrome, 47 per cent. with tincture of iodine and 87 per cent. with the metaphen solution.

3. Surface-skin disinfection of the unwashed human skin was obtained in 28.8 per cent. of tests with mercurochrome, 96.1 per cent. with tincture of iodine and 98.0 per cent. with the metaphen solution.

4. Deep skin disinfection (scraping tests) of the unwashed human skin was obtained in 3.8 per cent. of tests with mercurochrome, 84.6 per cent. with tincture of iodine and 94.2 per cent. with the metaphen solution.

5. No surface or deep skin disinfection was obtained on the purposely infected rabbit's skin or the unwashed human skin with a control alcohol-acetone-aqueous solution.

## CONCLUSION

This comparative study of pre-operative skin disinfectants has shown that the alcohol-acetone-aqueous 0.5 per cent. solution of metaphen is relatively free from the objectionable features of solutions of tincture of iodine and the alcohol-acetone-aqueous 2 per cent. mercurochrome and that it fulfills under strictly controlled conditions the requirements of an efficient and non-deleterious pre-operative skin disinfectant.

ADDENDUM.—After this paper had gone to press, the authors succeeded in eliminating from the alcohol-acetone-aqueous 0.5 per cent. solution of metaphen the objectionable features of instability on prolonged standing and precipitation of blood proteins in higher concentrations. The addition of 2.5 cubic centimetres of normal sodium hydroxide per 100 cubic centimetres of the formula employed in this paper, resulted in an initial heavy precipitation which immediately dissolved on further addition of the required alkali. Repetition of a smaller series of the experiments performed in the present report has demonstrated that the improved formula retains the values of the original formula as an efficient and non-deleterious pre-operative skin disinfectant, and that it remains stable in solution and fails to precipitate blood serum.

# DISINFECTANT VALUE OF METAPHEN

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# TRANSACTIONS

OF THE

## NEW YORK SURGICAL SOCIETY

STATED MEETING HELD MAY 14, 1930

The President, DR. EDWIN BEER, in the Chair

### BILATERAL BREAST CARCINOMA, OF LONG DURATION

DR. CHARLES E. FARR presented a woman, who in March, 1913, then forty-nine years of age, was admitted to the New York Hospital on account of a small tumor in the left breast which had first been noticed shortly before her admission. This tumor was hard, attached slightly to the skin but apparently not to the deep fascia. No axillary nodes were palpable.

A radical mastectomy of the left breast was performed, including the muscles and the axillary contents. Recovery was uneventful. She was discharged practically healed on April 9, 1913.

The pathological report is as follows:

Reported by Doctor Elser, March 31, 1913.

"Specimen consists of a rather large breast, left side. Three inches to the left of the nipple and on the level of this structure is a slight retraction of the skin. On section the breast shows numerous cysts filled with a grayish black fluid material. At one point corresponding to the depression referred to above there is a nodule irregularly ovoidal in shape, about the size of a pecan nut. Cut section of this nodule presents the typical characteristics of a carcinoma.

"Frozen sections made from this area confirm the diagnosis.

"The case is of special interest in that, according to the history, the opposite breast, it is claimed by the patient, developed a tumor some years ago which subsided without treatment. This suggests either a cyst formation or a mastitis in the opposite organ.

"Examination of the axillary contents fails to reveal enlarged lymph-nodes. Sections made from two small lymph nodes which are normal in size fail to reveal evidences of metastases."

This woman again entered the hospital February 20, 1925, complaining of a tumor in the right breast, which a few weeks before admission she first noticed.

Physical examination revealed scar of the left mastectomy. In the upper outer quadrant of the right breast was a discrete mass the size of an egg, which was adherent neither to skin nor underlying tissues. Nipple was not retracted. No axillary enlargement demonstrated. February 21, 1925, a radical mastectomy of the right breast was performed, including the axillary contents and the muscles. Again, the recovery was without incident.

The pathological report is as follows: Reported by Doctor Beattie February 25, 1925.

"Specimen consists of a moderate-sized fatty breast with a mass of induration about 2 centimetres in diameter at its outer border. On section this mass shows an irregular growth of yellowish white tissue, firm in texture, extending irregularly into the fatty tissue of the breast. In the attached muscle and connective tissue are found several hard lymph nodes varying in size from 3 millimetres to 1 centimetre in diameter. Microscopic section shows the picture of a carcinoma. The epithelial cells lie in irregular cords and nests and show hardly any tendency to form alveoli. There is a good deal of scar-like stroma. Section of lymph nodes shows inflammatory hyperplasia of sinus endothelium; no evidence of tumor metastases.

## ECHINOCOCCUS CYST OF LIVER

"Microscopic section of lymph nodes shows proliferation of endothelial cell lining sinuses, but no evidence of tumor metastases is seen."

The woman has remained in excellent health generally since this last operation and has no evidences whatever of recurrence or metastases. She never had any radiation treatment of any sort.

The slides made from the tumors in this case were reviewed by Dr. Lawrence W. Smith, of the Pathological Department of the New York Hospital in April, 1930. He was able to find a block of the tissue preserved in this case and to make a supplementary slide for further study. This study concurs in the original report of an extremely scirrhus carcinoma of the breast with infiltration of the fat tissue. The lymph-nodes show no evidence of tumor metastases.

## ECHINOCOCCUS CYST OF LIVER

DOCTOR FARR presented a woman, fifty-three years of age, who entered the New York Hospital in the service of Doctor Conner, October 25, 1929. Her chief complaint was pain in the hypochondrium, chills and fever. Her past history was of no bearing, except that for the past five or ten years she had had occasional attacks of pain in the left hypochondrium. These attacks came on every four or five months and lasted three to four days. They were accompanied by severe frontal headaches, but without visual symptoms. There was no jaundice, no vomiting in the attacks, but nausea was present occasionally. There was no radiation of pain to the shoulder or the scapula. There was a slight tendency to constipation. The last attack began three days before admission with severe pain in the left hypochondrium, radiating to the right hypochondrium, but not to the shoulder or scapula. There was slight jaundice, but no nausea or vomiting. There was no hæmaturia or dysuria. On the morning of admission she had a fainting attack of five minutes' duration.

Her temperature on admission was 104° F., pulse 124, respiration 44. The patient seemed stuporous, almost comatose. She was so obese that examination was almost useless, but there was a definite and rather marked tenderness in the left hypochondrium extending moderately to the right hypochondrium.

On the date of admission the leucocytes were 27,300 with 91 per cent. polymorphonuclears and 6 per cent. lymphocytes, 1 per cent. large mononuclears and 2 per cent. transitionals. There were no eosinophiles.

Operation was advised under the provisional diagnosis of acute pancreatitis. Under spinal anæsthesia with spinocain, a long right rectus incision was made. There was a small amount of free fluid. The gall-bladder was enlarged and thickened but contained no stones. In the left lobe of the liver posteriorly was a huge multicystic mass, much larger than a grapefruit, with many cavities, some of which seemed to communicate. The approach through the gastro-hepatic omentum was exceedingly difficult because of the great depth. An attempt at aspiration was negative. Finally packing was introduced and the largest of the cysts was incised. A large number of daughter cysts at once protruded. It was impossible to bring the cyst wall to the parietal peritonæum. The opening was therefore enlarged and about four ounces of daughter cysts, sac wall and membrane were sucked out. The cysts were further broken up with the finger and many more evacuated with the sucker. A large rubber tube was sutured into the cavity. Iodoform gauze packed around this and a Gibson-Mikulicz tampon completed the packing.

The patient left the operating room in fairly good condition. It was deemed impossible to treat this cyst by the injection of formaldehyde because of the great depth and the many individual cysts. Recovery was very tedious and stormy with many relapses of temperature, but there was gradual improvement after about three weeks and then another relapse for five or six days.

November 25, the patient was again removed to the operating room and under spinal anæsthesia an Israel incision was made in the left flank. The left lobe of the liver was freely exposed, but no evidence of renewed cyst formation could be found, nor any cyst wall which could be attacked. This wound was closed in part and drain inserted. It healed without any evidence of ever communicating with hydatid disease.

The patient left the hospital on the 13th of January, 1930, nearly three months after the primary operation, still with a discharging sinus. She has improved slowly in general health. Her wounds are healed. She has no symptoms. There is a beginning herniation in each of these unsutured wounds.

Doctor Farr then presented (through the courtesy of Doctor Langworthy) the statistics of echinococcus cyst of the liver shown by the First Surgical or Cornell Division of the New York Hospital, service of Doctor Gibson.

*Occurrence.*—In this series of seven cases of echinococcus disease of the liver, four of the patients were males and three were females. All were adults, the ages ranging from nineteen to fifty-three years, five being between twenty and forty. All were of foreign birth or had lived for many years abroad, two being Greek, two Italian, one Turkish, one Armenian and one Austrian.

*Symptoms.*—In every instance, the symptom which led the patient to seek treatment was pain in the upper abdomen. The pain was said to be constant in some cases and intermittent in others; it was usually dull in character and confined to the upper abdomen. This symptom had been present, at least intermittently, for several years in four cases (the four oldest patients) but for only two weeks to six months in three cases. That pain may be a relatively late symptom was evident from the extensive disease disclosed at operation in the cases with pain of only a few weeks' duration. The complaint of tumor as well as pain was given in only two of the seven cases, the tumor having been noticed four years before onset of the pain in one instance, and several months after onset of the pain in the other. Difficulty in breathing as well as pain was complained of by only one patient, who subsequently developed a subphrenic abscess.

*Physical Examination.*—Three patients appeared to be in good general condition, two appeared chronically, and two acutely, ill. Two had slight jaundice of the scleræ. A tumor was palpable in the epigastrium or right hypochondrium in three cases and visible as well as palpable in a fourth. Moderate enlargement of the right lobe of the liver, without palpable tumor, was noted in two cases, and in one case (an obese patient with cysts of the inferior surface of the left lobe of the liver) neither enlargement of the liver nor tumor was felt. Slight tenderness was present in the epigastrium or right upper quadrant in five cases, and some degree of muscular spasm in three. The so-called hydatid fremitus was elicited in one case only,

## DISLOCATION OF THE CARPAL SEMILUNAR

this patient having a large cyst close to the anterior abdominal wall. The temperature before operation was normal in two cases, slightly elevated in two cases ( $99.4^{\circ}$ – $100.8^{\circ}$  F.) and distinctly elevated in three ( $102.4^{\circ}$ – $104.2^{\circ}$  F.).

*Laboratory Examination.*—Radiographic examination of the abdomen (without pneumoperitoneum) was done in three cases and in these failed to show the presence of a tumor. A leucocytosis was present in four cases, this being slight (white blood cells 13,400) in one instance, and marked (white blood cells 18,500 to 27,300) in three. Of the six cases in which differential count of the leucocytes was made, three showed a slight increase and one a marked increase in the absolute number of eosinophiles.

*Pre-operative Diagnosis.*—A diagnosis of echinococcus disease was made in but one of the seven cases before operation. In two cases no pre-operative diagnosis was recorded, in one case the diagnosis was abdominal abscess, in two cases, cholecystitis, and in one case cholecystitis or acute pancreatitis.

*Surgical Treatment and Results.*—In three cases (all with single cysts) a two-stage operation was performed, an interval of four to five days being allowed between opening of the abdomen and incision of the cyst. Marsupialization and drainage was done in one of these cases, drainage plus irrigation with antiseptics in the second, and simple drainage with a tube, in the third. The first two patients were discharged improved after post-operative periods of twenty-four and forty-six days respectively. The third patient, who had had a severe hæmorrhage from the liver four days after the institution of drainage, died on the eighth post-operative day.

In three cases, laparotomy and incision of the cyst or cysts was done at one operation. One of these patients, with a single cyst, developed a subphrenic abscess necessitating a second operation five months after the first, but was discharged at six months, improved. Another of these cases, with multiple cysts of the inferior surface of the left lobe of liver, was subjected to a second operation one month after the first, with left posterior (Israel) incision to facilitate drainage, but still had slight fever when discharged to the out-patient department on the eightieth day. In the third case, which also had multiple cysts, the largest cyst only was incised and marsupialized. The patient was transferred after twenty-four days to another hospital, where he died about three weeks later.

In one case exploratory laparotomy revealed such extensive disease, and in such an inaccessible location, that surgical interference (other than biopsy) was not attempted.

## DISLOCATION OF THE CARPAL SEMILUNAR

DOCTOR FARR presented a man aged thirty, who entered the New York Hospital March 20, 1930, in the service of Doctor Gibson.

On December 26 he fell 23 feet on his right side and arm. From the time of the accident he was not able to move his right wrist or the fingers. He could, however, move the thumb. There was a marked loss of sensation in the hand. After ten days of home treatment sensation of touch returned, but up to the time of admission there was some numbness and recently

there was tingling in the fingers and hand. Two weeks before admission his fingers began to show some motion and power and he was able to make a fist. During these three months he never was able to move the wrist, which was kept in a straight and fixed position. In the region of the right carpus there was a painful swelling on the anterior surface over the semilunar bone, and a hollow on the dorsal surface in the corresponding position. All motions were painful and markedly restricted.

March 21 a vertical incision was made on the anterior surface, radial side of the wrist. The tendons were pushed aside. The anterior fragment of the scaphoid was removed. The semilunar lay in its proper bed in the radius but was dislocated from the os magnum. It was therefore removed and the os magnum then reduced with comparative ease. The wrist was put up in hyperextension. Closure with interrupted chromic, silk or skin. The time of operation was thirty minutes.

The X-ray report is as follows: "There is a fracture of the tip of the styloid extending into the joint. There is a disorganization of the proximal row of the carpal bones which seems to consist of a dislocated semilunar and



FIG. 1.—Dislocation of carpal semilunar bone.

fractured scaphoid. The film taken March 24, 1930 shows absence of the semilunar and the proximal portion of the scaphoid. The fractured radial styloid is clearly shown. (See Fig. 1.) Recovery was without incident. There has been fair progress toward return of power and motion.

DOCTOR FARR presented also a man, a laborer, who entered the New York Hospital March 26, 1930, in the service of Doctor Gibson. His complaint was of stiffness in the right wrist. February 18 while at work cranking a truck he wrenched his right wrist. It was painful and there was loss of function with swelling. The pain disappeared in a few days, but the swelling, stiffness and disability persisted. His history otherwise is without bearing.

There was definite limitation of motion in the right carpus, with an obvious deformity in the region of the semilunar carpal bone. There was a definite hollow on the dorsum, corresponding to this spot, and a swelling on the anterior surface. The pain and tenderness were very moderate.

February 27, 1930, an incision was made on the anterior surface toward the ulnar side. The carpal semilunar was found dislocated forward on its transverse axis and rotated laterally on its vertical axis. It was removed with considerable difficulty. The man made an uninterrupted recovery and is now nearing normal range of motion and power.

Doctor Farr stated that he had seen all told about thirty cases of dislocation of the carpal semilunar. One was bilateral. Only one case was seen early; this was easily reduced and the result was perfect. There have been

several late closed reductions, up to three weeks, with good results, averaging 80 to 90 per cent. return of function, and no pain. The results after removal of the semilunar for old unreduced dislocations are also good. No open reductions have been accomplished. Old unreduced and non-operated cases always have considerable disability, about 30 per cent., and pain, especially in bad weather. Nearly all of the cases are complicated by other injuries. Many have been entirely overlooked or treated as sprains. A little more care in the diagnosis and treatment of these apparently simple cases would save much suffering and disability.

#### STRANGULATION OF THE UNDESCENDED TESTIS

DOCTOR FARR presented an infant, born January 22, 1930, who was admitted to St. Mary's Hospital for Children on February 12, having developed a strangulated right inguinal hernia six days before admission. At frequent intervals the baby had vomited, especially during the last three days. For two days the parents had noticed swelling and redness along the right groin into the scrotum. This swelling had become much greater and more tense in the past twenty-four hours. The vomitus became very offensive (fæcal) and very frequent. No stool for twenty-four hours—very little for seventy-two hours.

The baby was operated on at once. An almost black, malformed testicle was found just below a strangulated loop of ileum in a congenital indirect hernia. The testis had just reached the superficial ring. It was freed from recent adhesions. The loop of ileum was freed and reduced with great difficulty. The sac was ligated and cut away, the cord dissected and testis placed in scrotum, although it seemed completely without circulation. The vessels were short and the testis just reached the top of the scrotum. A Bassini closure was performed without transplanting the cord.

Recovery was very stormy because of difficulty in feeding. Two whole blood transfusions were necessary. On one occasion the testis was exposed by a short incision to determine if it was the cause of the toxæmia. However, the testis seemed viable and was not disturbed. On discharge the infant had nearly regained its birth weight of 6 pounds, 14 ounces, and was in vigorous health.

Doctor Farr stated that this was the sixth case of strangulation of undescended testicle that he had personally operated upon. All the children recovered, although one died several months after operation from torsion of a loop of bowel. The testes were all sacrificed except this one. The diagnosis should be obvious because of the empty scrotal sac. The symptoms are those of partial or complete intestinal obstruction, depending upon the presence of a strangulated loop of bowel in addition to the torsion of the testicle. In two of these six cases there was no proof of torsion. The necrosis apparently followed either excessive pressure from behind or from a torsion which did not appear at operation. A considerable number of cases have been reported of late and in nearly all instances there is either a non-descent of the testis or malformation of the testis, or both.

#### FRACTURES AT THE CONDYLES OF THE FEMUR

DR. CONDUCT W. CUTLER, JR., read a paper with the above title for which see page 551.

## FIBROSIS OF COLON

DR. EDWARD D. TRUESDELL presented a man, fifty-four years of age, who had been in fairly good health until twelve days before his admission to hospital, when he was attacked with acute abdominal pain chiefly in the left lower quadrant, vomiting, diarrhoea alternating with constipation, and blood in the stools. For two months before the beginning of these symptoms he had noticed that he was constipated, quite frequently feeling a desire to go to stool but without result. At the time of his admission patient presented an acute abdomen such as would accompany a partial intestinal obstruction. His condition suggested cancer of the large bowel. Under palliative treatment the acute symptoms gradually subsided. X-rays revealed a linear narrowing of the descending colon and upper sigmoid. Wassermann was negative. Operation was performed November 7, 1929, three weeks after the onset of the acute symptoms. On opening the abdomen the pathology, so far as could be determined, was found to be limited to the descending colon. This had the appearance of a section of garden hose. The wall of the colon was constricted, thickened and dull red. The normal contour of the large bowel was absent, the portion involved having a column-like appearance. The lesion was sharply defined at its upper and lower limits and extended from just below the splenic flexure to the beginning of the sigmoid. The involved area was mobilized and excised and an end-to-end anastomosis performed. Examination of the specimen revealed no evidence of cancer or syphilis. Colon wall was greatly thrombosed, all coats being involved. The mucosa was necrotic in places. There was some fibrosis and infiltration of the colon wall by polymorphonuclear leucocytes. The veins of the mucosa and submucosa were greatly enlarged; the underlying lesion would seem to be more satisfactorily explained as perhaps an arterial one, there being a partial vascular obstruction due to thrombosis or embolism. The convalescence was uneventful; patient has gained in weight, bowels are regular, he has had no pain and declares himself to be better than before operation.

## BENIGN TUMOR OF STOMACH

DOCTOR TRUESDELL also presented a woman, fifty-nine years of age, whose past history had been uneventful, but who for four months past had suffered with what was considered to be "gall-bladder trouble." Three months before she had had an attack of acute pain in the upper abdomen, radiating to the right shoulder, with nausea, vomiting and slight subsequent jaundice. There had been persistent digestive disturbance. X-ray showed a faint gall-bladder shadow, which seemed to favor the suspicion pointing to trouble in the gall-bladder. At operation, January 11, 1930, the gall-bladder was found to be small, but not obviously diseased. No stones could be determined to be present in the biliary tract. A tumor was felt in the region of the pylorus which seemed at first to indicate the presence of malignancy. The tumor was found to be situated on the posterior wall of the stomach near the pylorus and projecting above the lesser curvature, being behind the anterior layer of the gastro-hepatic omentum. Division of the gastro-hepatic omentum uncovered a small round tumor resembling a subperitoneal fibroid. Tumor was attached to the posterior wall of the stomach but was readily enucleated, much as a subperitoneal fibroid is enucleated from the wall of the uterus. Tumor was  $2\frac{1}{2}$  inches in its greatest diameter and approximately an inch and a half in each of the other two. Pathological report showed the lesion to be a leiomyoma with some areas of myxoma probably derived from the muscle of the stomach wall. The recovery was uneventful and since operation there have been no further attacks of acute pain, there has been improvement in digestion and general health. Case was of interest because of the

symptoms first suggested gall-bladder disease and next malignancy of the stomach. Benign tumors of the stomach are not so rare as to be removed from consideration in patients with upper abdominal symptoms. While it seems that they occur in less than half of one per cent. of all stomach tumors, they are frequently reported. Groups of cases have been reported by several writers. Men and women are equally affected. Myomas are the most common type of benign stomach tumors. They are usually found in the region of the pylorus and may be sub-mucous, intra-mural or sub-serous, much as are myomas of the uterus. They may cause symptoms in two ways, either by interfering with function of digestion because of their obstruction to the motility of the stomach, or in other cases by occurrence of hæmorrhage. The tumor in this patient was so situated as to easily cause obstruction at the pylorus and at the same time to press upon the bile passage.

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STATED MEETING HELD OCTOBER 8, 1930

The President, DR. EDWIN BEER, in the Chair

#### ADENOCARCINOMA OF THE COLON SIGMOID

DR. G. A. CARLUCCI presented a woman, aged sixty-one years, who was admitted March 7, 1926, to the First Surgical Division of Bellevue Hospital with the complaint that the bowels had not moved for six days. She stated that she was naturally constipated but never went more than two days without a movement. This time her bowels had moved on March 1 and since then, in spite of repeated cathartics and enemas, she passed only a little gas and a few particles of fæces. She had not vomited, although she felt nauseated and complained of some pain in the lower left side of the abdomen. She had not passed any blood in the stools at any time. The abdomen is rounded, slightly tense and tympanitic. There is tenderness in the lower half and an indefinite mass can be felt in the left lower quadrant. Vaginal examination is negative and the rectal examination does not reveal the presence of a mass nor blood.

A laparotomy done March 13, 1926, revealed at the lower end of the sigmoid flexure of the colon an annular carcinoma about 3 centimetres long, not adherent to the surrounding structures. In the mesentery of the loop there were only two small palpable nodes felt. No nodes felt retroperitoneally. About 15 centimetres of the colon were removed. End-to-end anastomosis. Wound closed without drainage.

*Pathological Report.*—The resected piece of sigmoid colon was about 13 centimetres in length. On the external surface about 2 centimetres from the distal end is a constricting band which considerably narrows the diameter of the gut and this band feels indurated. The induration extends distally almost to the end of the resected gut. On section there can be seen corresponding to the distribution of the constricting band an annular growth which completely encircles the lumen and which is non-ulcerating. From the gross appearance the growth seems to extend in the muscular layers of the gut to within 0.5 centimetre of the distal end of the resected portion and it extends proximally for about 2 centimetres in the muscular layers beyond the limits of the constricting band. The constricting band proper is about 3 centimetres in length and almost occluded the lumen, the wall of the gut here being over 1 centimetre in thickness.

The microscopical examination revealed a mass of epithelial cells arranged in very definite alveolar formation extending through the muscular layers down almost to the serous surface and separated by dense bands of fibrous tissue.

*Post-operative Course.*—Highest temperature was 101°. She had very slight distention. Two bowel movements on the fifth day post-operative. No blood in stools. The abdominal wound healed by primary intention and patient was up on the eighteenth day.



She was then referred to the X-ray therapy department where she was given a course of deep X-ray treatments.

She left the hospital weighing 100 pounds and now weighs about 115. She has an occasional attack of constipation but an X-ray taken after a barium enema in May, 1928, shows no pathology four and a half years after operation.

#### ACUTE HÆMATOGENOUS OSTEOMYELITIS OF THE HUMERUS

DOCTOR CARLUCCI presented a man, aged twenty years, who cut his left foot on a piece of glass in March, 1926. The wound had become infected when first seen by the reporter about two weeks after the accident. He had an extensive cellulitis of the whole foot. He was taken to the Booth Memorial Hospital where several extensive incisions were made in the foot. The wounds were Dakinized and gradually cleared up so that about the end of April he was discharged in fairly good condition. Just before leaving the hospital he complained of some pain about his right elbow and a slight swelling there was noted. By May 15 he had developed a fairly high fever and a painful swelling of the whole shaft of the right humerus. An X-ray of the arm taken on May 18, 1926, revealed an acute osteomyelitis of the shaft with productive changes in the periosteum. The arm itself by this time was extremely hot, red and tender. He was readmitted to the hospital and under light gas-oxygen anæsthesia two incisions were made on the outer side of the arm and two fairly large drill holes were made in the shaft of the bone. Thick yellow pus was obtained from both openings. The holes were enlarged and then a long spiral probe was passed through from one opening to the other in order to establish through and through drainage. A rubber tube was then inserted in each opening in the bone and through and through irrigations were given, using a weak solution of zonite, every two hours.

He discharged freely from both wounds and apparently was doing quite well when about two weeks after the operation in turning his arm over to examine it the upper part of the shaft was fractured. The arm was kept in abduction on pillows without splints and the irrigations continued.

His general condition improved but he continued to discharge freely from both sinuses. An X-ray taken in July, 1926, demonstrated that union was taking place at the site of the fracture, that a good deal of the shaft was sequestering and that there was good productive reaction along the whole shaft.

October 4, 1926, X-ray showed solid union at the site of fracture and marked thickening of the shaft with areas of rarefaction. By this time he had begun to throw out pieces of the shaft and the lower wound was nearly closed but the upper one still was discharging pus.

He steadily improved thereafter continuing to throw out sequestra mostly from the upper sinus until March, 1927, the lower sinus was closed but the upper one led down to a cavity that apparently would not fill in. This sinus tract and cavity was opened and curetted out and then closed with sutures as there was no pus but just a mass of granulations. The wound healed with very little discharge and no other foci developed.

An X-ray taken November 27, 1927, and one taken September 18, 1930, show the subsequent reestablishment of the contour of the shaft to nearly its normal outline.

This case is reported on account of the severity of the infection, the method of treatment used, the unusual complication of a pathological fracture and the result four years following the operation.

#### PRIMARY (?) HODGKIN'S DISEASE OF THE SPLEEN

DOCTOR CARLUCCI presented a woman who when thirty-nine years old was first seen by him about May 1, 1927. She complained at that time of a

dragging sensation in the left side of the abdomen. She stated that she had had this sensation for the past eight years but that lately it had become worse progressively and it made her very uncomfortable if she stood too long or if she lay down on her right side. Recently she also suffered with nausea and nervousness.

She had not lost any weight and outside of this trouble she did not recollect any illnesses. No disturbance in the menstrual history. She has three grown-up children. She was a fairly well-developed woman in good general condition. In her abdomen could be felt a large mass in the left side that extended from the mid-costal margin downward to the iliac crest, smooth and rounded in contour. No tenderness. No rigidity. Liver edge not felt. No ascites.

Blood count: Hæmoglobin 79 per cent.; red blood cells 3,560,000; white blood cells 11,300. Differential: polymorphonuclears 76; lymphocytes 20; basophiles 2; large mononuclears 2. Smear for malarial parasites: negative. Blood Wassermann: negative.

She was admitted to the Misericordia Hospital where the spleen was removed. The splenectomy was fairly easy as there were only a few thin adhesions. After the operation she ran a fairly high temperature for about ten days but this gradually subsided and she healed by primary intention. Two other blood counts taken while she convalesced were 23,200 white blood cells with 88 per cent. polymorphonuclears, and 35,000 white blood cells and 76 per cent. polymorphonuclears respectively.

*Pathological Report by Dr. R. Schleussner.*—Specimen consists of a spleen measuring 28 by 16 by 10 centimetres, weighing 1700 grams. On section it is firm and elastic in consistency, has a smooth surface and shows obliteration of the normal markings. It is dull red in color. *Microscopic Section.*—The Malpighian corpuscles have in large part been destroyed and there is a diffuse fibrosis throughout. The splenic pulp is composed of lymphocytes with a smaller proportion of polymorphonuclears, leucocytes and large Dorothy Reed giant cells. There are no tubercles. *Diagnosis.*—Hodgkin's disease of the spleen.

The slides were also examined by Dr. Douglas Symmers who concurred in the diagnosis.

Following this report the patient was thoroughly examined for any glandular enlargements but none was found. She then went home and remained well for about six weeks when she began to have sever attacks of pain in the pit of the stomach accompanied by vomiting. These attacks would last several hours and then subside. About July 21 the pain became constant, radiating along the right costal margin and so severe that she was readmitted to Misericordia Hospital. At no time was she jaundiced. A cholecystogram taken at this time showed lack of dye in the gall-bladder and suspicious shadows, probably gall-stones. Physical examination was negative except for marked tenderness in the epigastrium. No masses felt.

Her pain persisted in spite of sedatives and she was finally operated on again, July 27. At this operation a very large, thickened gall-bladder was found with one faceted stone lodged near the cystic duct. No stones in the cystic duct but it was surrounded by several thickened lymph-nodes. In removing the gall-bladder severe bleeding was encountered due to two aberrant vessels near the cystic duct. This was controlled with difficulty and some packing was left in besides the cigarette drain.

The patient reacted well following this operation but she drained bile for over two months.

About the beginning of November, 1927, she again consulted the reporter, complaining of lower abdominal pains, frequency and burning of urination.

Her urine showed only traces of albumen and pus and no blood. Flat X-ray plates of the abdomen revealed no calculi. Vaginal examination showed a mass apparently involving the uterus and possibly the bladder. She was then referred to Dr. I. Kaplan who gave a course of deep X-ray treatments with distinct benefit.

Since then she has had several attacks of pain and swelling over the sacrum but they have been relieved by repeated X-ray treatments. Up to the present she has not developed any enlargement of the superficial lymph-nodes. The last blood count, taken in February, 1930, showed: hæmoglobin 80, red blood cells 4,910,000, white blood cells 27,900, polymorphonuclears 89, lymphocytes 11.

The case was shown on account of the rarity of the diagnosis of primary (?) Hodgkin's disease of the spleen. Although this cannot be positively proven in this case nevertheless there were absolutely no signs of any glandular hypertrophy at the time of the operation.

#### PERFORATED ULCER OF STOMACH

DR. FRANK B. BERRY presented a man, sixty-five years of age, who was admitted to Bellevue Hospital February 12, 1925. Well up to one year previously. Since then nausea and epigastric pain several hours after eating. This was relieved by bicarbonate of soda. One and a half hours before admission he had a terrific pain in the right upper quadrant of the abdomen. This pain was constant across the upper abdomen. Past history otherwise negative except for a large, easily reducible, right inguinal hernia.

Physical examination showed a markedly rigid and very tender abdomen, the signs most marked in the epigastrium. Temperature 100.2°; pulse 80 and regular; respiration 24; white blood cells 6,300; 73 per cent. polymorphonuclears; urine negative.

At operation a chronic ulcer, 1½ inches in diameter, was found with a perforation in its centre. A simple repair was performed; the patient made an uneventful recovery.

Indigestion and epigastric pain continued with diminishing force for about two months. Four months later it reappeared but was readily controlled by soda. One month later, seven months after his operation, he began to do hard manual labor and his pain increased.

He was readmitted to the hospital October 1, 1925. Gastric analysis showed a 600 cubic centimetres' retention of coffee-ground material. Temperature 98.6°; pulse 70 with extrasystoles; respiration 20; urine negative; blood-pressure 140/75. Blood: hæmoglobin 60 per cent.; red blood cells 3,100,000; white blood cells 9,600; polymorphonuclears 72 per cent.

At operation a large obstructing ulcer was found on the lesser curvature. In addition there were dense adhesions binding the whole anterior surface of the stomach to the diaphragm and under surface of the liver. The gastro-enterostomy was found to be well healed and functioning; there was no evidence of the former ulcer. The gall-bladder was large, thick walled, and covered with fibrin. Cholecystectomy was begun but the patient collapsed and his pulse jumped to 140 and was of poor quality. Therefore the operation was limited to a cholecystostomy. Culture from the gall-bladder was sterile. Patient made a good recovery and was discharged symptom-free and with a firm scar January 6, 1928. At that time his blood chemistry was normal.

He was seen in February, 1928, and complained of occasional headaches. These were relieved by medication. In October, 1928, he tried for the police force but was rejected because of his blood-pressure. He has continued to feel well and leads a perfectly normal life. In May, 1930, his blood-pressure

was 230/150 but the non-protein nitrogen in his blood was still normal—33 milligrams per 100 cubic centimetres.

This case was presented because of the unusual combination of conditions—hypertension in a man of twenty-seven, probable duodenal ulcer, and later acute cholecystitis, with relief following both of the surgical procedures.

## PERFORATED ULCER OF STOMACH—RESECTION

DOCTOR BERRY also presented a man, twenty-five years old, who was admitted to Bellevue Hospital August 26, 1925. For the previous six months he had had epigastric pain after meals and some belching. Shortly after lunch on the day of his admission he was suddenly seized with severe epigastric pain. Examination showed a general board-like rigidity of the entire abdomen. No other abnormalities noted. Temperature 98.8°; pulse 90; respiration 44; urine negative; white blood cells 9,200; polymorpho-nuclears 86 per cent.

He was operated upon about three hours after the onset of his symptoms. A large, indurated ulcer involving the pyloric portion of the lesser curvature of the stomach was found. It was adherent to the neck of the gall-bladder and on its anterior surface was a large rent admitting the tip of the thumb. The stomach itself was small and owing to the great surrounding induration and the friability of the tissues repair by simple means was impossible. Therefore the ulcer was freed from the gall-bladder and the distal 1/3 to 1/2 of the stomach with the ulcer was resected and a Pólya-Balfour type of anastomosis performed. Except for a mild post-operative pneumonia the patient made an uneventful convalescence and was discharged September 16, 1925, symptom-free and with his wound completely healed. In the first months after leaving the hospital he gained 25 pounds. At present, five years later, he eats, drinks and smokes whatever he wishes and drives a truck. There has never been any return of symptoms.

## CONCEALED CANCER OF THE TONGUE

DR. WILLIAM F. McFEE read a paper with the above title for which see page 481.

DR. FRANK S. MATHEWS referred to a case in which cancer of the tongue was not diagnosed until after the appearance of glandular involvement in the neck. The tumor even then was not easily seen on the back of the tongue but an induration could be felt with a central excavation by the examining finger.

DR. CHARLES GORDON HEYD said that in June, 1926, there came into his office a doctor, sixty years of age, with a white, glistening, hard "spot," about the size of the head of a pin, on the under surface of the left side of the tongue, at the junction of the anterior and middle third. On inspection it showed a red border and upon rolling the tongue between the tip of the first finger and the thumb of the right hand a hard, globular tumor could be palpated, approximately 5 centimetres in diameter. This was excised with a cautery knife, together with a wide encircling margin of normal tissue. It was submitted to three well-known and well-qualified pathologists who all reported the specimen as a basal-cell carcinoma. In view of the fact that there was a wide encircling margin of normal tissue, a point that was confirmed by the pathologists, it was deemed advisable to leave well enough alone. The patient had no evidence of recurrence in any way and was examined

from time to time. In May, 1927, or approximately eleven months after the excision of his lingual neoplasm, he appeared with a mass on the left side of the neck, about 5 centimetres below the level of the tip of the ear and posterior to the sternocleidomastoid muscle. This was superficial and there were no palpable glands between the symphysis of the jaw and this mass. The second neoplasm was excised and on examination by one laboratory was reported as a metastatic epithelioma. Two other pathologists reported a primary squamous-cell carcinoma of the skin and not metastatic. The patient and the specimens were then sent to Doctor Bloodgood, who said in substance that the tongue specimen was apparently one of the youngest cancers he had ever seen, that it was thoroughly removed and there was nothing to fear in so far as recurrence was concerned. On examination of the second specimen of the left upper neck he stated that it was a morphological cancer and not a physiological cancer—that it represented reaction of the skin to chronic irritation; that it was removed on all sides, less markedly underneath, but, he believed, thoroughly, and that there was no connection between the two tumors. It is now over four years since the excision of the lingual neoplasm and over three and a half years since the excision of the cervical neoplasm. The patient has had no recurrence and no disability, and has given no indication of any further trouble. This case indicates what may reasonably be expected when a malignancy in its very beginning is excised.

DR. JOHN DOUGLAS thought the point should be emphasized as to the absolute necessity of doing a biopsy in these cases. The most pathetic instances are those in which carcinoma of the tongue occurs simultaneously in cases showing positive Wassermann reaction, in which so long a time is taken up in treating the syphilis that by the time the lesion is discovered it is inoperable. If biopsy is done in such cases this mistake cannot occur.

DOCTOR McFEE, in closing, said that fortunately these were relatively benign cases. Otherwise he doubted if the patients shown would be alive today. To him an interesting part of this study was the relatively large proportion of women, fourteen out of seventy or 20 per cent. of this concealed type. It may be as common in women as in men, but as a rule one does not look for carcinoma of the tongue in women, and for this reason it may escape detection in a large per cent. of the cases occurring in women.

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STATED MEETING HELD OCTOBER 22, 1930

The President, DR. EDWIN BEER, in the Chair

STAPHYLOCOCCUS AUREUS SEPTICÆMIA

DR. HAROLD NEUHOF presented a boy, eight years of age, who was admitted to his service at Mount Sinai Hospital four days after the onset of high fever, some pain in the right leg in the region of the knee, and drowsiness. These manifestations had been persistent and progressive. The patient was said to have hurt his leg in some way several days before the onset of the symptoms. On admission the clinical picture was that of a

severe septic state with high fever, apathy, rapid pulse, slight cyanosis, several petechiæ on the forearms, and a palpable, soft spleen. There were physical signs in the chest suggestive of scattered metastatic foci in the lungs. There was a localized swelling, apparently slightly tender, over the upper right tibia, merging into an effusion in the knee-joint. The impression was given of a general septic invasion derived from the limited focus in the tibia, the osteomyelitic focus being no longer the essential part of the picture. Operation consisted of a simple incision and drainage of an abscess between the tibia and fibula, obviously derived from the tibia. No exploration of the bone was made. The administration of continuous intravenous glucose solution was begun and was carried on with little interruption for a period of twelve days. The amount of fluid administered daily ranged from 1000 to 6000 cubic centimetres, being varied according to the condition of the patient. Even on the fifth day after admission the blood culture contained colonies of staphylococcus aureus too numerous to count. Pericardial friction sounds appeared but the process did not go on to effusion. X-ray examination of the chest revealed the existence of bilateral pulmonary infiltrations with several areas of increased density suggesting multiple lung abscesses. These lesions cleared up spontaneously as noted by subsequent X-ray examinations. The patient's condition began to improve on the tenth day after admission although the temperatures still continued at a high level. The blood culture was negative on the fourteenth day. Operation for the osteomyelitis of the tibia was proceeded with when improvement was noted. Pus was evacuated from the bone. Some masses of necrotic bone were removed but no effort was made to clean up the focus entirely. A final operation was done when the patient was convalescent. This consisted in a thorough removal of necrotic bone and the detachment of several sequestra, resulting in deep excavation of the upper end of the tibia. The large cavity was packed. Altogether the patient ran temperatures for a period of six weeks, but the high fever with the general evidence of septic invasion lasted eleven days. After the patient left the hospital a sinus persisted and a revision of the wound has been necessary. Recently pain in the region of the left tibia appeared, lasting a few days. There was no temperature. An X-ray examination revealed a small area of rarefaction in the cortex. This represents a metastatic focus that was in all probability deposited at the time of the acute sepsis. Similar lesions may, of course, crop out at some future time.

#### ACUTE SUBMAXILLARY SIALADENITIS (LUDWIG'S ANGINA)

DOCTOR NEUHOF presented three cases of Ludwig's angina: First, a woman, forty years old, who was admitted to the Hospital for Joint Diseases with a three days' history of progressively increasing swelling beneath the chin, swelling in the floor of the mouth, and fever. The tongue was pushed upward and forward so that the patient had been unable to close her mouth for the preceding twelve hours. There was difficulty in swallowing. On physical examination the patient was obviously in great discomfort and breathed with difficulty. There was a diffuse, very obvious, and tender fullness beneath the jaw, more evident on the left than on the right side. Upon pressure over the left submaxillary region pus was noted to escape from the mouth of Wharton's duct. No similar discharge was noted upon pressure on the right side. A free incision was made with an exposure of the left submaxillary gland. Upon removal of the gland by severance of its duct, there was an escape of pus. By following the course of the duct a larger collection of pus was evacuated along the floor of the mouth. The infiltrated tissues were here laid open widely, placing a finger in the mouth beneath the tongue as a guide. The wound was lightly packed. Microscopic exami-

nation showed an acute suppurative inflammation of the submaxillary salivary gland.

The post-operative plan was to observe the progress on the opposite side and to employ the same procedure here if the lesion was progressive. However, there was rapid subsidence of the sublingual œdema with improvement in motions of the tongue, swallowing, and breathing. As the swelling on the right side subsided, a rounded, tender mass in the region of the right submaxillary salivary gland was felt. Upon pressure over the mass pus escaped from the mouth of the right Wharton's duct. The mass gradually subsided and at the time of discharge from the hospital six days after operation it had almost entirely disappeared. There was nothing unusual in the process of healing of the operative wound. There have been no subsequent symptoms referable to the right submaxillary region.

The second case was in the person of a girl who, when twelve years old, developed a painful swelling in the right submaxillary region during the course of measles. There developed difficulty in opening the mouth, in talking and swallowing, and it was no longer possible to close the mouth completely because of interference by the tongue. When admitted there was a large, diffuse, extremely tender mass occupying the entire right submaxillary region and extending over to the left of the median line. On attempting to open the mouth, the jaw was drawn to the right. The mouth could be opened only a short distance. The tongue was pushed upward by the mass beneath it and there was pronounced œdema of the sublingual mucous membrane. Upon pressure over the submaxillary mass, pus was seen to escape from the orifice of the right Wharton's duct. A free incision was made below the ramus of the jaw. Subcutaneously there was a widespread necrotic exudate. After this was traversed pus was found to escape from various points in the soft parts. A number of completely necrotic lymph-nodes were removed. When the dissection was deepened to the submaxillary salivary gland, most of this structure was firm and infiltrated, fixed by purulent exudate that encased it, and surrounded by small pus pockets. The gland was excised with considerable difficulty. The operative field then looked clean. However, upon following towards the floor of the mouth the probable course of Wharton's duct, an additional necrotic part of the gland was encountered and there was entered a collection of pus under tension that lay directly beneath the mucous membrane of the floor of the mouth. The wound was loosely packed. Microscopic examination of the salivary gland showed the presence of a widely disseminated, acute inflammation. The immediate post-operative course was characterized by a considerable necrosis in the depths of the wound. Injury of the lowest branch of the facial nerve was noted. While the patient was convalescent from the operation, an acute mastoiditis developed that required operation. The patient presents no symptoms referable to the submaxillary operation. Slight weakness in the ability to draw down the lower lip represents the residue of the facial nerve injury.

The third case presented by Doctor Neuhof was a girl who, when seventeen years old, was operated upon on his service at Mount Sinai Hospital for a ranula on the right side of the floor of the mouth. The operator noted that a duct-like structure was excised inadvertently in removing the cystic mass. The next evening difficulty in breathing was noted, the pulse became rapid and patient presented an anxious expression. The following morning there was great difficulty in breathing. The temperature was 101°, pulse 120. There was moderate cyanosis. The mouth could not be closed and the tongue was pushed upward by the swelling of the floor of the mouth. The region of the orifices of Wharton's ducts was in the midst of elevated œdematous mucous membrane that presented several patches of whitish

## ACUTE SUBMAXILLARY SIALADENITIS

exudate. The right submaxillary region was greatly swollen, tender, but the swelling did not extend over the ramus of the jaw. In the left submaxillary region a rounded, tender mass was felt in the region of and interpreted as the acutely inflamed left submaxillary salivary gland. Under a local anæsthesia a free incision was made below the ramus on the right side. Anatomical dissection was difficult because of the extreme restlessness of the patient and the rapidly advancing respiratory difficulty. After the platysma was traversed œdematous tissue was encountered in which a number of enlarged lymph-nodes were embedded. While the dissection was continued to expose the submaxillary salivary gland, the inspiratory stridor rapidly became worse. With one finger in the mouth beneath the tongue as a guide, curved scissors were bluntly introduced into the operative wound and pressed inward toward the finger. Odorless pus escaped. The track made by the scissors was rapidly split open and a finger was introduced which met the finger on the floor of the mouth, mucous membrane being between. The space occupied by the abscess lay along the lateral aspect of the floor of the mouth extending backward toward the pharynx. The wound was loosely packed. Slight improvement in the respiratory difficulty was noted shortly after operation. This was slowly progressive, but tracheotomy was impending for the first twenty-four hours. Thereafter, improvement in breathing was more rapid. The left submaxillary mass slowly subsided. Physical signs suggested the development of a small bronchopneumonic lesion and this was the only post-operative complication. Weakness of the right lower facial nerve indicated operative injury to the branches supplying the lower lip.

DR. RALPH COLP believed the term "Ludwig's angina" was a misnomer. It is not always an angina, and it was first described by Gensoul, of Lyon, in 1836. It was only later, when Ludwig treated the condition in Queen Catherine of Wurtenburg, that the term "Ludwig's angina" became known. It is a condition of phlegmonous infiltration of the alveolar tissues of the floor of the mouth. In the submaxillary region there are three distinct spaces as shown by Poulson, and later demonstrated by dissections in the department of dental anatomy at Columbia, namely the mylohyoid, the submaxillary, and the retromandibular spaces. Over half the cases of "Ludwig's angina" are simply infiltrations of the soft tissues of the floor of the mouth and the submaxillary gland is not involved. The submaxillary gland, however, whether involved or not, acts as a cork to these three spaces, and unless the salivary gland is removed, drainage is impaired. Almost immediately, and certainly within twenty-four hours, after gland removal, the distressing condition is relieved, especially the dyspnœa, and tracheotomy rarely is necessary.

DR. WILLIAM DARRACH asked if Ludwig in his original description of the condition bearing his name, included a suppurative condition of the submaxillary salivary gland. He was under the impression that Ludwig's angina was any phlegmonous condition in the submaxillary triangle. Because of the firm attachment of the deep fascia in this region, suppurative conditions in this part tend to spread to the floor of the mouth and then pass backward to the region of the pharynx and glottis. The subfascial space in the submaxillary triangle is separated from the floor of the mouth in front by the mylohyoid muscle. Behind the posterior margin of this muscle, the only obstruction to free communication between these two regions



is the submaxillary salivary gland. The greater portion of the latter rests on the mylohyoid and superficial to it. The gland, however, does extend posterior to the margin of this muscle and sends a deep prolongation of gland tissue forward with Wharton's duct on the buccal surface of the mylohyoid. In inflammatory conditions in this region, whether they start in the submaxillary lymph-nodes, superficial to the mylohyoid, or the buccal side of this muscle, that is beneath the floor of the mouth, free drainage of the latter space cannot be established through an incision in the submaxillary triangle unless the salivary gland is removed.

DOCTOR NEUHOF replied that from cursory reading he believed that the general impression held of Ludwig's angina is that it is a phlegmon extending from the floor of the mouth to the soft parts below the jaw associated with elevation and fixation of the tongue, difficulty in breathing and a rapid, often fulminating, progressive course. The customary operative procedure has been free incision or incisions through brawny tissue to the floor of the mouth. Pus is encountered in some cases and not in others. The pathogenesis of Ludwig's angina has been obscure in the case reports he has seen. The condition is not frequently encountered.

Doctor Darrach has described the more commonly met deep submaxillary suppurations requiring the removal of the submaxillary salivary gland in order to obtain adequate drainage of pus foci in that region. Although pus may be found around the submaxillary salivary gland in Ludwig's angina, *the removal of the gland does not suffice. It is the first stage in the dissection which should terminate in the opening of the pus pocket between the bed of the submaxillary salivary gland and the floor of the mouth.*

Doctor NeuhoF believed that his three reported cases give the lead to the pathogenesis of Ludwig's angina. In two of them pus was noted to escape from the orifice of Wharton's duct when pressure was made over the submaxillary swelling. In the third case the etiology was trauma due to an inadvertent removal of a portion of Wharton's duct at the operation for excision of a ranula.

In the first two cases the removed submaxillary salivary gland showed, upon microscopic examination, acute suppurative inflammation. Additional instances will have to be observed to prove that the pathogenesis of Ludwig's angina is an infection of the gland duct system. The findings in the only three cases seen in recent years, however, are highly significant in Doctor NeuhoF's opinion and give the lead for a precise surgical approach rather than the free incision method without any definite plan. The mortality of Ludwig's angina is very high and a precise plan of operative procedure may aid in its reduction.

#### PYÆMIA FOLLOWING TONSILLECTOMY

DR. HAROLD NEUHOF presented a woman, thirty-six years old, on whom tonsillectomy under local anæsthesia was performed July 15, 1929. There was an interval period of eight days during which she felt well. She then coughed and expectorated some bright blood and this recurred the next day. Eleven days after the tonsillectomy there was a sudden attack of coughing

with the expectoration of a large amount of foul green pus. Since that time profuse foul expectoration has continued and there has been constant fever. On admission to Mount Sinai Hospital there were the physical signs and X-ray evidences of a pneumonic infiltration in the right upper lobe in the midst of which a small cavity was noted in the X-ray film. There was little change in the physical signs and X-ray evidences for a month, when the lesion was noted to have progressed considerably and operation was decided upon. In that month's period the patient was treated bronchoscopically. Fever was irregular and the amount of foul sputum was never profuse. The first operation was performed December 13 under local anæsthesia. Portions of the second and third ribs were removed from the anterior chest wall and adherent pleura exposed. Pus was encountered by aspirating a short distance into the adherent lung. The latter was incised and the abscess cavity, lying a few centimetres from the surface, was entered by incision. There immediately followed a terrific hæmorrhage, blood gushing from the wound and pouring out of the mouth. Packings did not control bleeding. A finger was inserted to act as a tight plug and the patient was given a large dose of morphine. After she had quieted down the finger was removed, active bleeding had stopped, and the wound in the lung was tightly packed. The packing was kept in place for a number of days and was removed without any recurrence of hæmorrhage. The abscess cavity was found to be clean. Expectoration of foul pus continued. X-ray examination did not aid in locating additional cavities. For exploration for additional foci, eighteen days after the first operation, more of the second rib and part of the first rib were excised and the underlying adherent lung aspirated. Foul pus was encountered at a considerable depth in the apical part of the upper lobe. The infiltrated lung was laid open to enter the cavity and again active hæmorrhage was encountered, but not to such a degree as at the first operation. The cavity was firmly packed. The patient's condition improved after this operation and the sputum, although profuse, was no longer foul. Upon removal of the packing, the abscess cavity was found to be clean and there was a free bronchial communication. Severe diarrhœa developed, apparently the result of prolonged toxæmia, and was difficult to control. The temperature, normal in the immediate post-operative period, began to present occasional peaks up to  $103.5^{\circ}$ . Although the sputum was no longer foul, it became obvious that additional suppuration existed in the upper lobe. Accordingly, January 28 of this year, lipiodol was introduced into the bronchial fistulæ of the upper and lower wounds on the anterior aspect of the chest. This demonstrated by X-ray a path proceeding posteriorly to a pocket in the posterior aspect of the upper lobe. To reach this abscess in the paravertebral region, a vertical incision was made between the transverse processes of the second and third dorsal vertebræ and the mesial border of the scapula. Portions of the second and third ribs were excised just lateral to the transverse processes. Adherent pleura was encountered. The lung was aspirated through this and a large collection of foul pus was entered. The abscess cavity was laid open freely with relatively little bleeding. The cavity was of large size and was packed and drained. After this operation cough and expectoration progressively diminished. Diarrhœa gradually subsided as the patient's condition slowly improved. There then developed pains in the lower extremities, more marked on the left side, together with paræsthesiæ. These manifestations progressed for several days, reached a peak in about a week and then very slowly subsided. They have never completely disappeared. On examination neither dorsalis pedis was to be felt and the left posterior tibial pulse was absent. The popliteal pulsations were reduced, as were the oscillometric readings. As the thoracic wounds closed down a

path was found between the anterior and posterior entrances into the upper lobe. Through this a silk ligature was carried, the ends being tied over the shoulder. The purpose was to permit the wounds to narrow down but not as yet to close until all evidences of pulmonary infiltration had disappeared. The patient left the hospital in May in good condition and almost symptom-free. Since then she has remained well except for occasional discomfort in the lower extremities. There is still a cough and occasional expectoration of small amounts of mucoid material. The examination of the lower extremities reveals partial return of arterial patency. The maintenance of the track by the silk strand will soon be discontinued because a recent examination of the lower extremities indicates little pulmonary infiltration.

#### PYÆMIA WITH MULTIPLE ABSCESES

DOCTOR NEUHOF presented a man, thirty-six years old, who came under observation at Mount Sinai Hospital stating that he had been well until ten days before admission. At that time he began to complain of weakness, sore throat, cough, and pain in the left pectoral region and in the right lower chest. His physician noted a temperature of  $104^{\circ}$  and an injected throat. The next day the patient was up and about, but five days later he complained of generalized pains over the whole body but especially in the left pectoral region and axilla. He was unable to abduct his left arm more than halfway to the horizontal. Shortly thereafter a severe chill followed by high fever occurred and the pain in the left pectoral region disappeared. In the four days before admission there were three additional chills after the first two of which the temperature rose to  $107^{\circ}$ , to rise to  $108.5^{\circ}$  after the third chill. For two days before his admission pain in the middle finger of the left hand was noted. When the patient first came under observation in the hospital, a healed crusted patch was noted on the left thumb. Upon inquiry the patient recalled that there had been a *small blister in this region at the onset of his illness*. He recalled no cause for it and stated that the blister ruptured spontaneously, some cloudy fluid escaping. A blood culture taken shortly after admission was found to be positive, the organism being the hæmolytic streptococcus. During one week's observation the patient had several chills, the high septic temperatures rising on one occasion to  $108.2^{\circ}$ . A metastatic lesion over the right elbow appeared. A tender swelling in the left axilla was noted. At the end of a week the mass beneath the pectoralis became much more obvious upon forcible abduction of the left arm. The sequence of events was thought to be as follows: Infection derived from the bleb on the thumb or possibly some other unrecognized portal of entry on the hand; subpectoral abscess, suppurative phlebitis of the axillary or subclavian veins; septicæmia. A free incision was made that completely traversed both pectoral muscles. A large amount of pus, eight to ten ounces, was found beneath the pectoralis major, sacculated in three pockets lined by gray diphtheritic membrane. The lowest pocket was deep to the pectoral muscle, the second extended upward to the site of the axillary structures, and the third lay above the axillary vessels and nerves reaching to the clavicle. There was a shelf of inflammatory tissue between the two upper collections. This was in the region of the axillary vein. It was traversed, found to contain several acutely inflamed lymph-nodes, and led to the site of the lesion in the axillary vein, whose second portion was expanded, white, and contained a thrombus that could be felt through the unopened thick-walled vein. Further dissection of the vein disclosed an uninvolved first portion proximal to the site of the thrombus. Similarly the lesion tapered off into the third portion of the axillary vein. The wall

## CÆCOSTOMY WITH PROLAPSE OF CÆCUM

of the vein was firmly embedded in dense tissue agglutinating it to the surrounding structures and partly to the axillary artery. The branches of the vein appeared free from involvement. As the complete dissection of the vein was begun a ligature was thrown around the first portion to prevent any systemic invasion from fragments of the thrombus. The excision of the vein proved tedious because of its fixation to the surrounding structures. After the vein was freed it was tied off at its junction with the brachial below and removed in one piece. The specimen showed a suppurating thrombus about 5 centimetres long, broadly adherent to the wall of the vein. Its mesial end was rounded, the distal end rather sharply cut off. The whole wound was widely packed.

After operation temperatures ranged between  $100^{\circ}$  and  $105^{\circ}$  for the first week, dropping toward normal with occasional rises in the second week. There was no recurrence of chills. Blood culture became negative. The patient was placed upon continuous intravenous glucose solution begun directly after operation and given without interruption for several days. It was discontinued when the patient showed obvious improvement. A rapidly developing effusion in the right shoulder joint when aspirated revealed pus that contained hæmolytic streptococci. This lesion gradually subsided spontaneously. Several abscesses in the soft parts required incision. The metastatic lesion in the phalanx of the second finger of the left hand subsided spontaneously. A mass in the neck appeared, apparently derived from the hyoid bone, increased in size with some fulness in the pharyngeal wall, and was incised when found to be frankly fluctuant. The post-operative temperature was obviously due to the various abscesses that appeared, and possibly in part to the pulmonary process. From the X-ray examination of the latter it was impossible to determine whether the lesion was pneumonic or referable to suppurative foci. It subsided spontaneously. There was progressive healing of the axillary wound and the patient was discharged after a transfusion given for the anæmia, six weeks after operation. There have been no untoward phenomena since that time and function at the left shoulder is satisfactory.

## CÆCOSTOMY WITH PROLAPSE OF CÆCUM: ILEO-RECTAL ANASTOMOSIS

DR. GUILFORD S. DUDLEY presented a man twenty-eight years of age, who, in 1927, had been submitted to a cæcostomy for the relief of rectal polypi. Since that time all bowel movements had taken place through the cæcal opening and the cæcum had prolapsed about 4 inches from the abdominal wall. For the relief of this condition, he was admitted to Bellevue Hospital March 21, 1930. Examination gave evidence of a chronic ulcerative colitis with stricture of the rectum about 6 inches above the anus. Laparotomy done May 1, 1930, revealed a tight, annular scar tissue stricture of the left colon at the level of the pelvic brim; no other abnormality of intestines or liver was discovered. A lateral anastomosis was made between the terminal ileum and the rectum. After a stormy convalescence, he was discharged from the hospital at the end of seven weeks thereafter. Two months later he was re-admitted. At this time the greater part of his feces were being passed by the normal route but still a considerable amount escaped through the cæcostomy opening. September 15 the prolapsed cæcostomy was dissected free and the ileum separated from the cæcum.

The excess of cæcum was removed and both lumens closed with inverting sutures. It was hoped that the recto-sigmoid stricture was sufficiently patent to allow the passage of whatever mucoid secretion occurred in the excluded colon.

Convalescence from this procedure was marred only by the twelve to fourteen daily bowel movements per rectum. This frequency was diminished somewhat by the use of bismuth and tincture of opium. He now averages two to three defecations daily; is maintaining his general nutrition well; and despite the fact that he has no colon from which to absorb fluids, insists that he drinks no more water than an average individual. The cœcostomy has remained closed.

### CHOLECYSTOGASTROSTOMY FOR CHRONIC PANCREATITIS

DOCTOR DUDLEY presented also a woman sixty-six years of age, who was admitted to the Second Surgical Division of Bellevue Hospital March 18, 1930. She gave a three weeks' history of upper abdominal fullness and distress; anorexia; "sour stomach" and belching of gas. Three days before admission she experienced sudden sharp pain in the right upper abdomen and on the night before admission suffered an exacerbation of this pain which radiated to the right shoulder posteriorly and was accompanied by vomiting. Examination showed a slight icteric tint to the sclerae and skin; marked tenderness in the right upper abdomen; and a fever of 100°. She was kept under observation for ten days, during which time her jaundice at first increased but later decreased in intensity. On the day of operation very slight jaundice persisted. The laboratory reported a negative Wassermann reaction; a non-protein nitrogen of 38; blood sugar of 82; icteric index of 35; Van den Bergh direct immediate, indirect positive. X-ray after administration of dye showed the gall-bladder faintly visualized but no stones.

At operation March 28, 1930, the gall-bladder was found involved by moderately dense adhesions and its walls considerably thickened. There were no calculi palpable within the gall-bladder or its ducts. The entire pancreas was enlarged, nodular and of very firm consistency. It gave the distinct impression of being carcinomatous. There were no nearby enlarged lymphatic glands nor were there any metastatic deposits in the liver. Recognizing that this pancreatic change might also be the result of chronic inflammation, dependent in turn upon chronic infection within the biliary system, prolonged drainage of the gall-bladder would most adequately meet either situation. As drainage into the intestinal tract seemed more desirable than simple external drainage, a suture anastomosis was performed between the fundus of the gall-bladder and the pyloric antrum of the stomach. Her convalescence was uneventful and she left the hospital on the seventeenth post-operative day. Her subsequent course has been one of continued improvement. She has had no recurrence of biliary symptoms, has remained free from jaundice, and has gained in weight.

DR. HAROLD SANTEE said that his experience with cholecystogastrostomy comprised four cases. He found it satisfactory in cases where there was a question of carcinoma and chronic pancreatitis. If Doctor Dudley would describe the pathological condition representing carcinoma and the one representing simple pancreatitis, he said it would be possible to differentiate them. Occasionally a case presents diffuse inflammation with involvement of the head of the pancreas, and this is put down as chronic pancreatitis. The nodular feel and the complete extent of the involvement in others make one think they are carcinoma. A permanent drainage of the biliary tract would seem to determine the correctness of the solution of the problem. This case of Doctor Dudley's, however, would seem to have been a chronic pancreatitis. Doctor Santee had always been satisfied with the results of cholecystogastrostomy in these questionable cases.

## FRACTURE OF LEG; GAS BACILLUS INFECTION

DR. JOHN E. JENNINGS said that he had had considerable experience with cholecystogastrostomy, and he was not sure he would use it in every case with an indurated pancreas head. In many cases, drainage of the common duct would help to distinguish the morbidity and would relieve the cases of chronic pancreatitis. Doctor Jennings had seen some of these cases going about their work in the third hundred days, carrying small T tubes in the common duct, without any disturbance at all. In similar cases cholecystogastrostomy had not been so satisfactory as far as the gastric disturbance was concerned. The time, however, to decide the question was with the case open before the surgeon.

## MULTIPLE SKELETAL EXOSTOSES

DR. GUILFORD S. DUDLEY presented a man, twenty-one years of age, who first entered the Second Surgical Division of Bellevue Hospital in January, 1930, complaining of a tender swelling on the inner aspect of the lower portion of the right upper arm. He attributed its presence to an occupational injury received one and one-half years earlier. The swelling has not increased in size during this time and he sought treatment merely because of the handicap to his desired activities as a pugilist. Examination showed a walnut-sized, moderately tender, bony, hard swelling, apparently attached to the humerus at the junction of the latter's lower and middle thirds. X-ray showed this swelling to be an exostosis 4 centimetres in length and 2 centimetres in width. January 25, 1930, the mass was exposed and readily removed with a chisel. It appeared to have arisen from the shaft of the humerus on a line with the intermuscular septum between the brachialis anticus and the internal head of the triceps muscles. He was re-admitted to the hospital in September, 1930, complaining of soreness and stiffness in the left thigh after his "road-work," as well as pain and rapid fatigue upon injury to the inner aspect of the arm which had been operated upon eight months before. X-rays at this time showed an exostosis on the lateral aspect of the middle third of the left femur about twelve centimetres in length; a small exostosis just below the mid-point of the shaft of the right humerus (site of the previous operation); and a smaller exostosis on the shaft of the left humerus about  $2\frac{1}{2}$  centimetres from the shoulder-joint. The patient had been unaware of this last noted condition. There were no cranial exostoses.

September 22, 1930, the femoral exostosis was removed. It gave every clinical evidence of being identical in structure with the humeral exostosis. At the present time no further treatment is contemplated.

## FRACTURE OF LEG; GAS BACILLUS INFECTION

DR. ROBERT H. KENNEDY presented a man, aged twenty-four, who, December 17, 1924, when eighteen years of age, was struck on the right leg by cardboard weighing 100 pounds. When admitted to the Beekman Street Hospital he presented a large wound at the junction of the middle and lower thirds of the right leg. The X-ray photograph showed also a badly comminuted fracture of the tibia at the junction of the middle and lower thirds with one large, loose piece displaced outward and another inward. There was a transverse fracture of the fibula  $3\frac{1}{2}$  inches below its upper epiphyseal line, the lower fragment being displaced backward and inward. Under general anæsthesia a débridement of the wound was done after thorough cleansing and the tibial fracture was reduced manually through the wound. The wound was closed and plaster splints applied.

Within twenty-four hours signs of gas bacillus infection were present

and this was proved bacteriologically. The wound was immediately laid open and Carrel-Dakin treatment instituted. The patient was also given 400 cubic centimetres of tetanus perfringens serum intravenously. During the second day there was no progress of the gas bacillus infection. On his fifth day there was no evidence of gas bacillus infection but there was extensive purulent infection between the muscle planes. The leg was incised widely to above the knee-joint and Carrel-Dakin treatment instituted throughout.

On the twelfth day a Steinman pin was inserted through the os calcis, chiefly for greater ease in dressing the leg, and traction instituted. Up to the end of his fourth week further incision was made every few days for abscess formation. During all this period it was expected that amputation would be necessary. After four weeks improvement commenced and at forty-seven days the tibia showed a large amount of callus. The traction was removed on the fifty-fifth day, although the union was not solid. On the seventy-third day he was allowed up in a chair and by this time had flexion at the knee to 90 degrees. On the eighty-sixth day a secondary suture was attempted for the large open wound over the tibia, but this was only partially successful. The union of the tibia is noted as being solid on the one hundred and third day. On the one hundred and eleventh day Thiersch grafts were applied to the remaining open wounds. He was discharged on his one hundred and thirty-second day with wounds healed, solid union, practically complete motion at the knee-joint and almost no active motion at the ankle-joint. He was walking with crutches and with no splints on. He was bearing full weight at seven to eight months. At fifteen months he returned to part-time work.

January 10, 1929, more than four years after the first admission, he was again admitted to the Beekman Street Hospital with a painful swelling on the external aspect of the heel of five days' duration. This was incised and about one dram of thick pus evacuated. In the depth there was a depression in the os calcis about 1 centimetre deep, being apparently the site of entrance of the Steinman pin. The roughened overhanging bone was curetted away and the wound was entirely healed in two and one-half months and has remained so. Otherwise there had been no sequestration. He had no complaints, no shortening, and no loss of function except that he could dorsiflex the foot to 90 degrees only.

Doctor Kennedy also presented a man, aged thirty-seven, a porter, who was admitted to the Beekman Street Hospital February 20, 1924, at the age of thirty-one. He had caught his right leg between an elevator and its shaft and sustained a compound, comminuted fracture of both bones of the leg in the middle third. He was given a general anæsthetic and after the wound was cleaned it was débrided and a fragment of tibia 2 inches long removed. One end of the tibia was then engaged in the medulla of the other end. The wound was left open, Carrel-Dakin treatment instituted and plaster splints applied.

Three days later gas bacillus infection was evident and the leg was laid open from 2 inches below the knee to the internal malleolus. He also received 400 cubic centimetres of tetanus perfringens serum intravenously in twenty-four hours. The infection was promptly controlled and by the eighteenth day the wound was fairly clean and commencing to epithelialize. He was allowed up in a chair on the twenty-ninth day and commenced to use crutches on the fifty-eighth day. He was discharged on the one hundred and seventh day with union. At present he has no shortening, no deformity of bone and complete function of knee and ankle. The leg is smaller than that of the opposite side. He did not work for one and one-half years at the end of which time his compensation case was settled, giving him 95 per cent. loss

## FRACTURE OF LEG; GAS BACILLUS INFECTION

of leg. His regular work was as a tailor and at the time of the accident he was working as a porter temporarily. He is now employed as a tailor earning more money than before the accident. This patient was shown as a late result in a severe compound comminuted fracture complicated by gas bacillus infection; also because of the method used in locking the fragments. It is of interest to compare the 95 per cent. loss of leg awarded by the compensation board with the late result.

Doctor Kennedy also presented a man, aged thirty-seven, who was admitted to the Beekman Street Hospital May 4, 1927. He had fallen on the sidewalk, sustaining an oblique fracture of both bones of the leg in the middle third, not compounded. The X-ray taken in emergency traction showed good position. There was a spur which seemed likely to engage and hold the fragments in position. The leg was therefore put up in plaster splints. The next X-ray showed that the fragments had slipped and on the fourth day traction by tongs in the malleoli was instituted. On the ninth day the tongs slipped and a Steinman pin was inserted through the os calcis. This was removed on the forty-third day, and plaster splints applied. He was then allowed up on crutches. On his sixty-sixth day the X-ray showed practically no callus and a false point of motion was still present. He insisted on going home and signed a release. The splints were removed four months after injury. He used two crutches up to six months and after nine months walked without a stick. Knee motion was complete at six months and ankle motion at eight months. The pin holes closed before he left the hospital and never gave him any trouble. At one year he returned to his usual work at usual pay. He shows a slight anterior bowing of the tibia with a lump at the site of fracture. There is no shortening, function is perfect and he has no complaints. This case illustrated the common experience in the slipping of oblique fractures and the necessity of more than mere immobilization if healing is to be obtained without shortening.

DR. ROBERT H. KENNEDY then read a paper entitled "Fracture of the Shaft of Both Bones of the Leg. An Analysis of One Hundred and Seven Cases," for which see page 563.

DR. WILLIAM DARRACH remarked with reference to the relative frequency with which Doctor Kennedy had used reduction by plaster and reduction by traction. There were many in this group in which, Doctor Darrach believed, Doctor Kennedy would now use traction. The cases of oblique fracture, where plaster was put on and failed of results and then traction was used, illustrate the experience of many surgeons with oblique fractures. Where traction can be used and watched carefully, one gets better results than from simple reduction and use of plaster. When the ends can be made to engage and lock, the traction method may not be necessary. There are several things that have been learned about traction, by bitter experience, and one is that it should not be considered a method of treatment all by itself, but should be used with manipulation of fragments. Also, if one is going to get reduction by traction, one must get it early. Doctor Darrach believed that with a given fracture, if traction was put on within one hour of the injury, five pounds might bring it down; ten pounds in two hours, or fifteen pounds in six hours. Twelve hours afterward it might take twenty to twenty-five pounds. The result, however, will be much better with a strong pull at the start. Doctor Darrach often starts right away with



thirty pounds' skeletal traction, and within thirty-six hours reduces it. If the purpose has been accomplished within six to twelve hours, the pull can be reduced, getting down to fifteen pounds as soon as possible. In many cases one can get lengthening but not apposition of fragments with traction alone. Fragment should be replaced by manipulation within twenty-four hours. Traction should be used in connection with old-fashioned manipulation of fragments, either by fingers alone or by pressure from without. What Doctor Kennedy said was true, that traction requires as much attention and experience as open operation—perhaps even more so. With traction one is never done, for constant care must be taken with adjustments.

Another surprising thing was the length of time this group of cases took for solid union. This is more in common with experience than with the textbooks, which speak of getting solid union within six weeks. Experience shows it is more likely to take twelve weeks in spiral fractures, or eight weeks in fractures of the lower third. In most of the textbooks the description of the time taken for solid union is far too optimistic. There was only one point in which Doctor Darrach disagreed with Doctor Kennedy, and that was the way in which he spoke of non-union. He thought it was not fair to talk of non-union until after a year. Delayed union, yes. In severe cases with soft-part injury, the normal time for union may be six or eight months.

DR. DONALD GORDON said that this group of cases demonstrated a cross section of some very conscientiously cared-for cases in this city, from the time of first aid to the time of the follow-up. It furnished a very excellent comparison for men doing fracture work, rather rare at the present time. Most of the complications appear to have been due to damage of the soft parts. They seem to have been handled extremely well. These cases emphasized the need of greater attention to the immediate care of the damaged soft parts. Six or seven years ago, at the City Hospital, the speaker, with Dr. Howard Collins, realized that spiral fractures required traction, but found that the tongs then in use were unsatisfactory. Doctor Collins designed a simple parallel bar device which consisted of two round parallel metal bars nine inches long, which are held apart parallel to each other by two flat metal members eight inches long, also parallel to each other. The flat members cross the round bars at right angles, and are attached to these by four adjustable locking connections. The connections permit separation of the round bars, rotation on their long axis, and a difference in length from the cross member where the traction cord is applied to the pin which enters the malleoli. In one end of each round bar there is a hole at right angles to the long axis which receives a steel pin  $1\frac{1}{2}$  inches long and  $\frac{3}{16}$  inch in diameter. This is held in place by a small thumb screw. This pin has a rounded tip instead of a sharp one (a suggestion of Dr. Kirby Dwight). After a small skin incision is made, a hole is drilled in the outer cortex of each malleolus with a  $\frac{3}{16}$ -inch drill. The blunt pins are introduced, the bars adjusted to the pins and locked in position. The blunt pin does not grove its way out under traction, and cannot penetrate. The adjustment takes care of the superior and anterior position of the internal malleolus,

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and of any discrepancy in the angles of the drilled holes. It permits some movement of the ankle-joint. This devise was used with considerable success on a case of intractable spiral fracture. It offers a suggestion for further work on these lines.

DR. JOHN J. MOORHEAD remarked that the Steinman nail was regarded as the best form of skeletal traction. This has been the experience at the Post-graduate Hospital. In regard to the cases of delayed union, in his experience this has occurred more in fractures of the lower third of the tibia and fibula than in any other part of the body. A point of interest was the early reduction accomplished in these cases. Starting reduction when the case is first seen by a staff trained to regard these broken bones as emergency cases, in the same way they regard appendicitis, is very significant. As to the method of estimating the end-results in the Post-graduate Hospital, they had been using for a number of years a method that seemed simpler. Instead of taking the three factors which they have at the Massachusetts General Hospital, anatomical, economic, and functional, the Post-graduate estimates the end-results in terms of function, union, and contour. It remains to give function, union, and contour statistical value. By function is meant capacity to perform, by union is meant the state of repair, and by contour is meant external appearance. By giving statistical value to these, one can come to some sort of numerical value. Therefore function is estimated at 60 per cent., union at 20 per cent., and contour at 20 per cent. If to a patient half his former function is restored, it is estimated at 30 per cent. Half union is put at 10 per cent. and half contour at 10 per cent. The sum of these three would be a 50 per cent. end-result.

DR. SETH M. MILLIKEN said he had used the traction method for years in all cases where maintenance of reduction was difficult. He had seen no damage to the ankle from the use of the pin in the os calcis as muscular function, which was kept up by the balanced traction, promptly restored the joint separation. He emphasized the fact that a maximum weight must be applied at first; that is, sufficiently heavy to reduce the fragments promptly, by distraction if necessary. As soon as over-riding is corrected the weight may be reduced until only sufficient is used to maintain the alignment, the surrounding muscles maintaining the apposition.

DR. KENNEDY, answering Doctor Neuhof's question, said that tetanus perfringens serum had been used in at least twenty-five gas bacillus cases. It was always accompanied by thorough surgical incisions. It had no ill effects and may have had some good ones. It was used sometimes as a prophylactic in cases in which there was a possibility of gas developing. Replying to Doctor Murray, he said that scrubbing in débridement of these wounds had produced no ill effects. They were wounds which were dirty from being dragged in the streets or ground in the bottom of an elevator shaft. When there was no marked muscular injury, an effort was made to get out the dirt rather than cut out muscle. If there was actual dead muscle, that was naturally cut away. Great dependence was placed on thorough washing, irrigating with up to 3 to 5 gallons of fluid.

# BRIEF COMMUNICATIONS

## THIOCRESOL IN WOUND HEALING

FURTHER experience with thiocresol has confirmed the thesis that the sulphhydryl radicle stimulates cell division. The reasons for this and a technic for the use of thiocresol in wound healing were given in a previous communication.<sup>1</sup>

A most important fact in this field is that the new skin covering a recently healed leg ulcer, for example, is very thin, shiny, translucent and delicate. This, coupled with the poor circulation so often in the neighborhood, is a real threat to durable healing. Appropriate methods to aid circulation can be used, such as bandages, elastics, heat, *etc.*, and perhaps central stimulants



FIG. 1.—A. Skin of left shoulder of albino rat. Painted 3x weekly with 1 per cent. cresol in alcohol. B. Skin of right shoulder of the same rat. Painted 3x weekly with 1 per cent. thiocresol in alcohol. Both photomicrographs of parafin, H. and E. sections x95.

when necessary. Thiocresol can be used to stimulate the new skin to material thickness. At the same time increase in vascularity occurs beneath.

The evidence for this statement was first obtained in rats and mice.<sup>2</sup> The hair was carefully clipped and various percentages of thiocresol in both alcohol and in lanolin were rubbed on the intact skin. After about six weeks, applications being made three to six times a week, the skin was grossly and microscopically thickened to four and five times normal. (Fig. 1.)

Successful experience to date in humans was obtained in three cases, two of leg ulcer, one of ulcer of the side of the foot. A description of the latter follows:

Mrs. C., now aged thirty years, was injured twenty-one years ago (in 1909) by a heavy weight falling on the outer side of the left foot. A bruise resulted and large vessels were probably severely injured, from the history of the extensive ecchymosis. The part remained tender and sensitive. Fourteen years ago (in 1916), an ulcer

## THIOCRESOL IN WOUND HEALING

appeared which healed several times after rest, skin grafting and other surgical procedures, but only for short periods of time. On examination in May, 1930, an ulcer several years old, 5 by 6 centimetres by 0.5 centimetres, presented a fairly clean, dull brown-red base and hardened, slightly inverted edges. The skin surrounding was pigmented light brown, slightly oedematous, poorly vascular. Treatment with 1:10,000 solution of thiocresol resulted in complete healing in three weeks. The epithelium covering the old denuded area was thin and delicate. The patient was anxious lest a



FIG. 2.—Mrs. C's foot—(d) Line of extent of the ulcer at various times; (c) operative-scars; (b) line of extent of the ulcer in May, 1930; (a) thickened skin localized to area rubbed with 0.25 per cent. thiocresol in lanolin.

slight trauma again break the surface. One-quarter of one per cent. thiocresol in lanolin was rubbed in three times a week. In three weeks the new skin was thicker to the touch than the normal skin of the foot, though freely movable over the underlying fascia. Its color and reaction to momentary pressure showed good vascularization. (Fig. 2.)

In using the stronger concentrations of thiocresol in rats and mice, it was noted that a proportion (about 20 per cent.) of the animals developed

small vesicles and papules on the area treated after about two weeks of applications. Finally scabs, fissures and excoriations appeared. In spite of continued application of the thiocresol, these healed after about two weeks, and the end-results at six weeks in both the animals which developed the eruption and those which did not, were the same, *viz.*, much thickened skins.

Of fifteen laboratory workers who have been in contact with the chem-



FIG. 3.—Hand of a "sensitive" laboratory worker after exposure to 1 per cent. alcoholic solution of thiocresol. The stopcock broke off a burette containing the solution; it spilled over the hand; was not washed off for some time. Composite picture of a week's duration; the small vesicles like ivy poisoning appeared first and were followed by coalescence to large blebs. Treatment with boric acid ointment containing 0.5 per cent. menthol allayed the itching, and healing took place in about two weeks. This is the extreme case of those observed.

ical, two have shown the same phenomenon. Naturally, in their cases, they were removed from the exposure.

That it was not the organic portion of the molecule, *i.e.*, the cresol portion of thiocresol, which was responsible, is shown in animals by the fact that control applications of equivalent concentrations of cresol to the same

## THIOCRESOL IN WOUND HEALING

animals, on other parts of their skin, at the same time, showed no effects whatsoever.

Also, other sulphhydryl-containing compounds produce the same results, *e.g.*, benzyl mercaptan.

In the two laboratory workers and in six patients to date, the untoward reaction can be described as follows: In two patients, the 1:10,000 solution produced the phenomenon (applied three days and seven days, respectively); in the others, stronger concentrations (0.25 per cent. to 1 per cent.) were used but once. Small papules rapidly becoming vesicles appeared on the reddened surface of the skin. They itched intensely and in two cases were diagnosed as ivy poisoning by physicians who knew nothing of the history. The distribution was sharply confined to the area of skin to which the thiocresol was applied. The vesicles coalesced in two to three days to larger or smaller blisters. (Fig. 3.) The itching ceased. The blisters on puncture released a clear yellow serum and healing went on, uninterrupted. Points of difference from ordinary burns are the intense itching and when the blisters were excised, the exposed surfaces were not raw and red, but pink and apparently no more sensitive than the surrounding skin. In addition, stronger alcoholic solutions (up to 5 per cent.) when deliberately applied to the skin of several "non-sensitive" volunteers, produced no caustic effects.

Since it is quite clear that cell-division results depend on concentration, time, and number of applications, we now use 0.1 per cent. thiocresol in lanolin for further experience in thickening the skin. It is very likely the optimum concentration varies with individuals.

Obviously, this "hypersensitivity," so to speak, is worthy of intensive investigation. The theoretical basis and biological significance will shortly be discussed from this institute.<sup>3</sup>

### SUMMARY

Applications of stronger concentrations of thiocresol (0.25 per cent. in lanolin, for example, three times weekly), will cause cell proliferation and thickening of the skin, with increase in vascularity in the subcutaneous tissues.

The skin of a certain percentage of individuals reacts to these stronger concentrations by vesicular eruptions which later disappear.

Weaker concentrations may be better adapted in certain cases.

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## APPENDICOVESICAL FISTULA

FOREIGN bodies are considered to be an infrequent cause of appendicitis, especially in America, where the faecalith is not regarded as a foreign body. A survey of the literature (Mitchell,<sup>1</sup> Fowler<sup>2</sup> and Berger<sup>3</sup>) shows that approximately 2 to 3 per cent. of all cases of appendicitis are caused by true foreign bodies. Mahoney<sup>4</sup> reports a series of seventy-four cases in which foreign bodies were the cause of appendicitis. In forty of these cases the appendicitis was due to the presence of sharp instruments (pins), and the mortality in thirty-eight was 55.2 per cent. In the majority of these cases the appendicitis occurred in childhood, and no history of swallowing the pin could be obtained.

Keen<sup>5</sup> reports the case of a man aged twenty-four, who had suffered from dysuria since the age of seven years. At the onset of the dysuria the



FIG. 1.—Vesical calculus from incrustated pin.

family doctor found a pin in the urethra and removed it. The patient stated that he did not insert the pin into the penis, nor did he remember swallowing it. At the age of twenty-three he was thought to have a rectovesical fistula secondary to the rupture of a prostatic abscess. Two unsuccessful attempts were made to close this fistula. One year later a laparotomy was performed and a long appendix was found, with its distal end incorporated into the bladder wall. The appendix was separated from the bladder and removed, and the patient made an uneventful recovery.

## CASE HISTORY

The patient, a man aged twenty-six years, entered the clinic on June 17, 1930, complaining that he had been troubled with bladder stones since 1917. He had been treated by irrigations for a very painful bladder, and had been cystoscoped twice with negative findings. The patient states that in January, 1925, he fell downstairs and "jarred a stone loose from the bladder wall." An X-ray picture taken at that time revealed a large stone in the bladder surrounding a pin (Fig. 1). This was removed

## APPENDICOVESICAL FISTULA

from the bladder one week later. The patient did not recall swallowing the pin, but his mother stated that it had been swallowed when he was about six months old.

In January, 1926, a recurrent calculus was removed from the bladder by cystotomy, and in July, 1927, a third stone was removed *per methram* by means of a lithotrite. During 1927-1928 the patient suffered intense pain with each urination. During the preceding two years he had attacks of chills and fever, and passed gravel and blood in the urine. Several times these attacks were accompanied by pain in the region of the left kidney, and during the preceding month he had noticed a material in the urine that looked like faeces.

X-ray examination revealed no suspicious shadows in the genito-urinary tract. On cystoscopic examination the bladder was found to be very much inflamed. In the posterior portion of the bladder near the top there was a depression which suggested a fistula connecting with the bowel. Considerable faecal material was found in the bladder, suggesting the existence of an enterovesical fistula. In view of the badly inflamed bladder, retrograde pyelograms were not made. Uroselectan was given intravenously, and the urogram showed moderate right hydronephrosis, with a normal ureter.

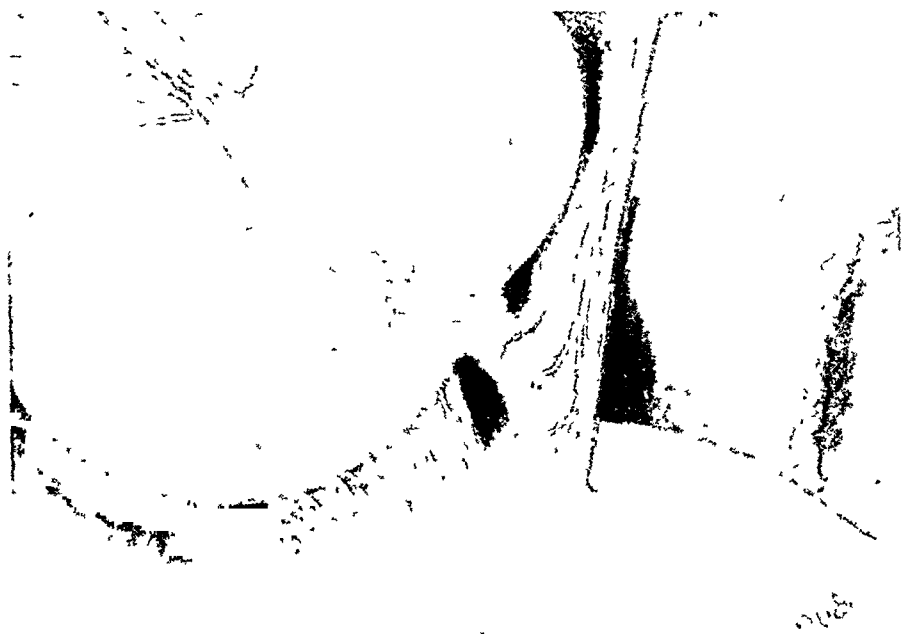


FIG 2—Drawing showing the appendix and its attachment to the bladder.

The left renal pelvis appeared to be normal. The left ureter was visualized, but not well visualized, and was normal. The bladder was small but normal.

The patient entered the hospital June 28, 1930; a suprapubic operation was done on the 30th, under spinal anaesthesia. After the small intestines had been packed off into the upper abdomen. The appendix was found adherent to the dome of the bladder (Fig. 2). The enterovesical fistula was in all probability due to the pin swallowed by the patient in infancy which had lodged in the appendix and perforated the bladder. The appendix was removed from the cæcum, and its distal end dissected free from the bladder wall. The bladder was closed by inverting the wall with two rows of continuous catgut sutures.

The pathologist reported that the specimen consisted of a portion of the appendix which was adherent to and communicated with the bladder. On one surface it was lined by soft, velvety, irregular mucous membrane such as is seen in the bladder. The surrounding portion of the tissue showed dense fibrous adhesions. Opening into the centre of the patch of mucous membrane was a small tubular structure which allowed the passage of a probe. This was the appendix. (Fig. 3.)



After the operation the patient made an uneventful recovery, and was discharged in two weeks. A month later he returned to the clinic, reporting that he was free from symptoms. The urine was clear, amber colored, and alkaline in reaction. The specific gravity was 1.020. It contained neither albumin nor sugar, and the microscopic examination of the urine gave essentially negative findings.

In reviewing the literature, only one other report was found of a case of appendicovesical fistula. However, although reports of such cases are rare, the presence of foreign bodies in the appendix is not uncommon.

Urologists frequently find foreign bodies in the bladder, but it usually is believed that they have been inserted into the urethra, slipped beyond the patient's control, and ascended to the bladder. Once there, they become encrusted with mineral salts and a calculus is formed. When our patient stated that a pin was found in the bladder, we supposed

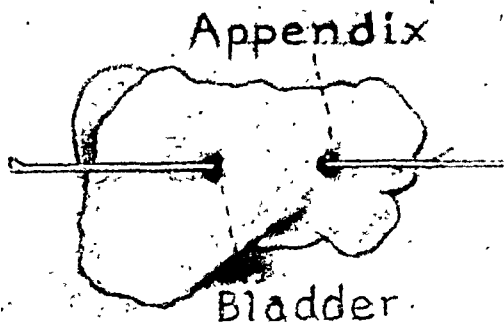


FIG. 3.—The fistulous tract excised showing the connection between appendix and bladder.

that it had been introduced through the urethra, but subsequent events in his case led to the belief that the pin swallowed in infancy lodged in the appendix and penetrated the bladder, causing an appendicovesical fistula. The bladder stone with the pin was removed in January, 1925, but the fistula persisted, and was the cause of the re-formation of the bladder stones. Since the removal of the appendix and closure of the fistula the patient has been free from urinary symptoms.

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#### SUPERNUMERARY ECTOPIC URETER

THIS case is reported: (1) To record an extremely rare anomaly. (2) To submit the pathological evidence for the first time that this type of

## SUPERNUMERARY ECTOPIC URETER

supernumerary ectopic ureter is explained by persistence of Wolffian body and not by splitting of ureteral analgen. (3) To plead for conservation of kidney to which this structure is attached so intimately that nephrectomy at first seems indicated.

A woman, aged twenty-two years, presented herself, complaining of continuous loss of urine with occasional severe attacks of pain in right kidney region. She was married at nineteen, had a baby at twenty-one years of age. Since birth has continued to have enough loss of urine to necessitate wearing two pads each day. Occasionally she suffered a typical kidney ureteral colic consisting of severe pain in right kidney which radiated into vagina and inner aspect of right thigh. Pain was followed by chills, fever, nausea and vomiting. It was unusual in that a vaginal discharge often occurred during or soon after these attacks. The attacks had durations of from two to eight days and were not relieved by morphia which always made vomiting more severe. Discharge after



FIG. 1.—Injection of accessory tube with sodium iodide.



FIG. 2.—Injection with 12½ per cent. sodium iodide. Showing relation of accessory tube and kidney.

the attack was like "lochia" or "like milk," and continued for about twelve days after the initial escape of about four tablespoonfuls. Her treatment had extended over twenty years and many procedures had been tried, including dilatation of urethral and ureteral strictures for two years, kidney lavage, bladder irrigations, douches, removal of appendix, and fixation of right kidney through a lumbo-lateral incision. None of these procedures seemed to influence the escape of urine, and the attacks of colic were increasing in severity and frequency.

She was a well-developed woman; there was no odor of urine. General examination was negative except for a tender oblique scar of kidney incision. Genito-urinary examination revealed the apparently normal genitalia of a multipara. Uterus and adnexa normal, urethra not remarkable. Posterior to the urethra about two millimetres and about one millimetre to the right of the mid-line between two folds in anterior vaginal wall, an opening not unlike a second urethra was found and entered with a small probe for about one-quarter of an inch. The tract became tortuous or strictured at this point.

## BRIEF COMMUNICATIONS

Indigocarmine was injected intravenously and appeared in three minutes in bladder urine; did not appear in excretion from this abnormal opening however.

*Cystoscopic Examination.*—Bladder interior not remarkable except that the trigon seems small, landmarks not well developed. There is a low-grade trigonitis. Ureters

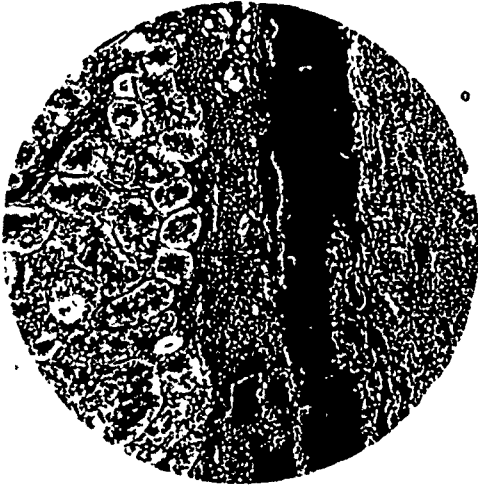


FIG. 3.—Normal kidney adherent but not connected structurally to tube.



FIG. 4.—High power of epithelium and submucosa.

were catheterized, appearance time, phthalein output and urine equal and satisfactory from both kidneys. As catheterization of the abnormal opening in the vagina was not possible, sodium iodide 12 per cent. was injected by means of a urethral syringe into sinus tract and the contrast media was also injected into ureteral catheters simultaneously and X-rayed. The films demonstrated normal kidneys and ureters and in addi-



FIG. 5.—Lymphoid nodules and gland-like structures not unlike those found in intestinal tract.



FIG. 6.—Stratified transitional epithelium and low cuboidal epithelium-lined tube.

tion, an accessory tube with a bulb-shaped end internal, posterior, and superior to, the right kidney. The tube wound itself around the normal ureter, crossing it twice as it descended to the vagina where it was very tortuous and showed alternating dilatations and strictures. Injection of this tube reproduced the typical colicky pain of which patient complained. Laboratory findings have never been remarkable though they included Wassermann, blood and urine, and an attempt was made to determine the exact character of fluid escaping from the accessory ureter. The smear did show pus cells

## SUPERNUMERARY ECTOPIC URETER

and diplococci, Gram-negative, coming from the ancestry ureter but fluid could not be identified as urine.

*Operation.*—Through the usual lumbo-lateral kidney incision, the kidney and ureter on right side were exposed. Previous fixation of kidney to twelfth rib made dissection difficult. Normal kidney and ureter were displaced forward and accessory tube about diameter of index finger identified by palpation and aspiration. Upper third of ectopic ureter was dissected from vena cava by clamping many small veins that ran directly to it from vena cava. One large vein which ran directly to the upper pole of kidney was ligated and divided. Upper third of tract was resected and left in relation with the pole of kidney, part of upper pole of kidney was covered after covering incision in kidney with fat tissue to prevent cutting of stitches and to insure good closure and hæmostasis. Kidney was replaced in fossa and dissection continued toward vagina. The grapevining of the tube around the normal ureter was now beautifully demonstrated. Dissection was continued beyond the brim of the pelvis. Accessory ureter was excised and removed.

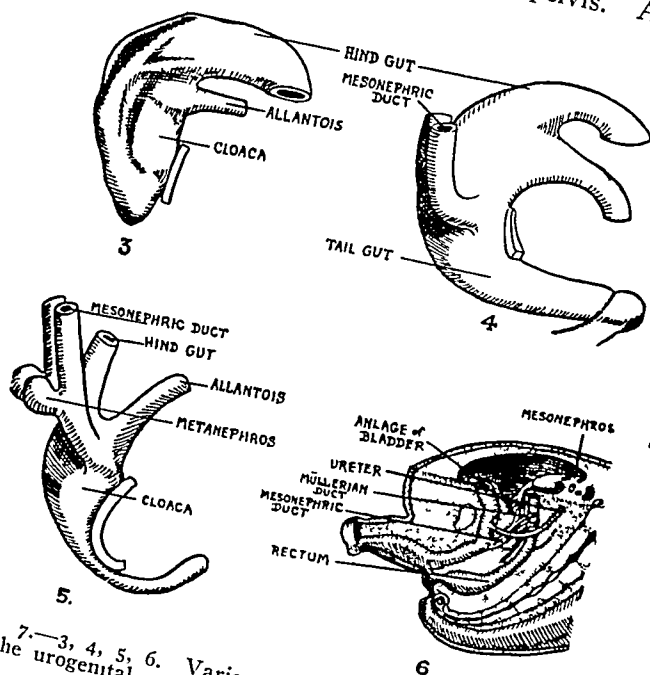


FIG. 7.—3, 4, 5, 6. Various stages in the development of the urogenital system. (After Prentees and Avery.)

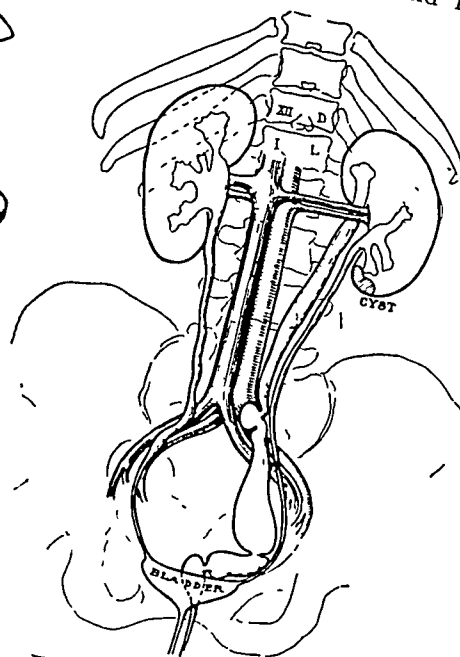


FIG. 8.—Diagrammatic reproduction of structures as found by examination and at operation, showing supernumerary and normal kidney, pelvis and ureters.

Stump was ligated with chromic catgut and cauterized with carbolic acid. Carbolic acid was also injected into lumen of stump to insure sterilization, destruction of mucosa and encourage obliteration. Wound was closed in layers, catgut for muscle, chromic for fascia, silkworm figure of eights for retention and dermal for skin sutures. Two penrose drains were left in wound. Patient made an uneventful recovery.

*Pathological Examination.*—The specimen consists of a long tubular structure measuring twenty-four centimetres in length and from one to two centimetres in breadth. The upper end is bulbous and ends as a blind tube. A portion of kidney tissue is attached laterally to this bulbous end of the tube. The tube walls are thin and lined with mucous membrane which has been stained by methylene blue. The kidney is firmly attached to the tube by adhesions but on section there seems to be no structural connection between the kidney and tube.

Microscopically, the tube consists of several layers, the mucosa, lined with an epithelium that varies from a columnar single-celled layer, as found in the intestinal tract,

to a stratified transitional epithelium resembling that found in the bladder. In the sub-mucosa, the second layer, masses of lymphatic tissue, also gland-like structures resembling intestinal glands, are found. The remainder of the tube consists of a circular muscular layer and a longitudinal muscular layer surrounded by adventitia. There is a marked inflammatory picture as shown by the small round-celled and plasma-celled infiltration.

Spitzer and Wallin in *ANNALS OF SURGERY* for December, 1928, suggest that embryologically this can be interpreted as a retention of mesonephric tubules and Wolffian duct rather than older explanation of splitting and reduplication of original kidney band on Wolffian duct, and offer the following reasons to substantiate the contention. 1. Gärtner's ducts in females are remnants of Wolffian body and these ureters opened in the position of Gärtner's ducts. 2. Excretion is probably not urine. 3. That pelvis is poorly developed and mesonephrotic structure and not kidney tissue is connected with accessory tube.

They stated that the problem would probably ultimately reach solution should a careful histological study ever be available. We concur in their opinion that this strange body is not a ureter but an adult Wolffian system—a persistent mesonephric duct and Wolffian body, and for the first time, submit pathological specimen and microscopic study to substantiate this interpretation. This investigation reveals: 1. That connection with upper pole of kidney may be by adhesions only and not by collecting tubules. 2. That epithelium may vary from intestinal type of columnarepithelium to stratified transitional epithelium which should not occasion surprise as analgen is derived from cloaca. 3. That mucosa contains intestinal-like glands and lymphatic tissues that suggest intestinal structure.

While reduplication of ureter with unusual implantation is relatively rare, about one hundred cases having been reported, this particular type is *very* rare.

Kilbane in his article in *Surgery, Gynecology and Obstetrics*, January 1926, records two cases in Table IV which probably could be similarly classified had the histological material been available. Full credit should be given to Spitzer and Wallin for indicating necessary study to prove that reduplication of ureter and persistence of mesonephric duct are two distinct entities. The resulting surgical problems are radically different. For reduplication of ureter, ligation, pyelopyelostomy, transplantation into bladder or bowel and heminephrectomy have all been suggested or tried. But in this newly recognized condition, though the picture may be similar the anomaly should be dissected from the kidney and entirely removed. Plea is therefore made for conservation of kidney, though at the time of operation kidney may seem to be structurally a part of Wolffian body.

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## THE USE OF FASCIA LATA FOR THE OCCLUSION OF ARTERIES IN CASE OF ANEURISM

IN THE ANNALS OF SURGERY of July, 1930, vol. xcii, No. 1, pp. 8-22, J. M. Hanford and J. M. Wheeler, writing about pulsating exophthalmos, are discussing the different methods of arterial occlusion. The great danger of immediate complete and permanent occlusion of the common or internal carotid artery, especially with older people, is too well known to be commented upon. This is why in 1911 Matas and Allen advocated the technic of *partial* occlusion by an aluminum band, which could be compressed completely at a second operation. About the same time Neff reported his method of *gradual* occlusion by placing the artery between the two blades of an aluminum clamp, which are gradually approximated by the traction of rubber bands. With both methods a second operation is necessary; in the first instance, to make the complete occlusion, in the latter, to remove the clamp. H. H. Kerr, in 1925, reported three cases, in which he used with good success a strip of fascia lata for the *partial* occlusion of the common carotid artery for pulsating exophthalmos, after two to four weeks followed by a complete ligation. Thus in all these cases a two-stage operation was done systematically and no use was made of the tendency of the fascial band to shrink, thus gradually producing a complete occlusion out of a partial one; in his second case he reoperated, although after two weeks the subjective and objective signs of the disease were very much diminished after the partial occlusion, which operation might have been unnecessary. This tendency to shrink and produce after a while a complete occlusion out of a partial one is attributed also to the chromicized pig's bladder (Baer's membrane) by Hitzrot and in the case reported by Hanford and Wheeler this seemed to have happened indeed. Especially where an occlusion of the common or internal carotid artery is necessary it is of the utmost importance to give the collateral circulation a chance to develop, that this be done *very gradually*; and it seems to me that the fascial band, on account of its above-mentioned property and because it is tolerated very well by the tissues permanently, is the ideal material to use in these cases. Even if no complete occlusion would ensue by itself, one can make a complete ligation later with much less danger, because the collaterals are in the meantime gradually trained to take over the work.

To illustrate this shrinking tendency of a fascial band, by which an aneurism of the brachial artery with insufficient collateral circulation was cured after a partial ligation, I wish to report the following case:

December 10, 1925, a girl, nineteen years old, consulted me for a swelling at the inner side of the right arm, which had been discovered a few months previously by chance. It had not given her any trouble at all and since then it had not grown perceptibly. As far as she knew no trauma had occurred in this region. Examination revealed an aneurism of the right brachial artery, about four centimetres long and two centimetres in diameter, somewhat below the insertion of the deltoid muscle. The expansile pulsation disappeared when the artery above it was occluded by pressure. The radial pulse was, although smaller than at the other side, distinctly palpable. The reaction of Wassermann was negative. With a palpable pulse in the artery below the aneurism

one could already predict an insufficiency of the collateral circulation, but for all security the test according to Matas was done, which proved to be negative (no hyperæmic reaction occurred after removing the elastic compression with the artery above the aneurism still occluded).

Under these circumstances a complete and sudden ligation of the artery was certainly courting disaster; in one or the other way we had first to improve the collateral circulation before contemplating this. It then occurred to me that we could make a *partial* ligation of the artery above the aneurism with a strip of fascia lata and thus force the collaterals to do more work and become better developed, after which an extirpation of the aneurism could be done with impunity.

December 11, 1925, I operated under local anæsthesia, removing a strip of fascia lata, six centimetres long and one centimetre broad, from the outer part of the thigh and bringing this under the artery just above the aneurism; the two ends of the fascial band were pulled upward and then a straight artery clamp, catching these between the jaws, and placed parallel with the artery, was pushed up against the artery as far as possible and locked; then a second similar clamp was placed between the first one and

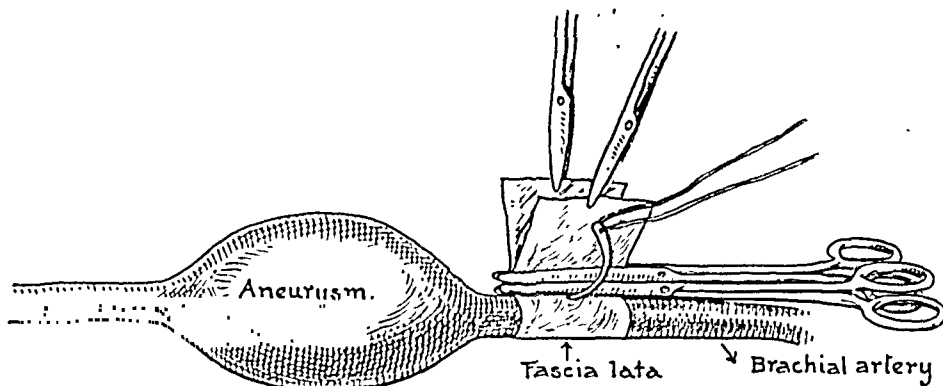


FIG. 1.

the artery, after which the pulsations in the aneurism and radial artery were just palpable; then a round needle with a double silk ligature was brought between the second clamp and the artery, both ends of which, after cutting the loop, were brought back in the same way through both margins of the fascial band and tied securely while the clamps were removed (see the drawing). After ascertaining that the circulation in the arm and hand was sufficient the wound was closed without drainage. For a few days the right arm was kept somewhat elevated and, although the arm and hand felt a little colder than at the opposite side, at no time were there any signs of trouble with the circulation. Ten days after the operation, for the first time, there could not be felt any pulsations in the aneurism or radial artery; about a month after the operation the aneurism had shrunk to about half of its former size and still no pulsation was felt here, but this time the radial artery could be felt pulsating, although faintly, which could in no other way be explained but that the collaterals had developed and brought the blood from the brachial artery above the aneurism through the arteriæ collaterales ulnaris superior-collaterales media and radialis via the rete articulare cubiti and arteriæ collateralis ulnaris inferior and recurrens radialis back to the radial artery. This was further substantiated by the test of Matas which proved now to be distinctly positive. During a few months after the operation the patient complained of becoming tired easily in the right arm, which then felt cold also, but these signs of somewhat impaired circulation soon disappeared altogether and the last time I heard from her about a year ago, she had no trouble at all with her arm, even after playing a strenuous game of tennis. The former aneurism has changed into a small hard (fibrous) nodule.

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## URETERAL ABDOMINAL WALL TRANSPLANTATION

### THE EXPERIMENTAL TRANSPLANTATION OF THE URETERAL ORIFICES TO THE ANTERIOR WALL OF THE ABDOMEN

TRANSPLANTATION of the ureters into the wall of the abdomen provides an easy method for the differential study of renal function in animals, and the difficulties of cystoscopy are obviated. The transplantation may be done in one or two stages. Such preparations are entirely satisfactory if care is taken to prevent subsequent infection of the urinary tract. The chief advantage of the method lies in the ease with which the ureters may be catheterized and with which the intact animal may be studied. Catheters large enough completely to occlude the lumen of the ureter may be employed and hence all leakage about the catheters prevented. Under such conditions quantitative study of the urine can readily be undertaken.

The following technic for the transplantation of the ureters into the

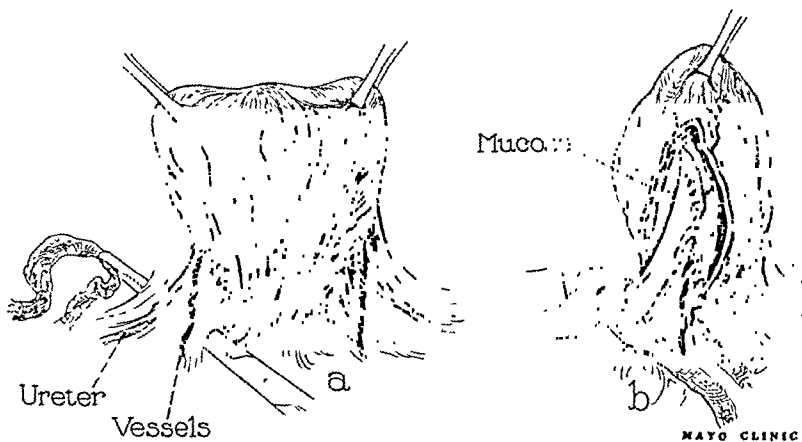


FIG. 1a.—Method of isolating the ureter and the accompanying blood-vessel, and b, sectioning the muscularis.

abdomen of the dog has been so uniformly successful that it seemed worthy of description.

Under ether anæsthesia and with strict regard for asepsis, a median-line suprapubic incision is made. The bladder is delivered out of the wound, and the adjacent viscera and the margins of the wound are carefully protected by packing. An opening is made by blunt dissection through the thin areolar tissues at a point near to the neck of the bladder and immediately subjacent to the ureter which is to be transplanted. A strip of gauze is pulled through the opening. The gauze not only protects the ureter, and particularly its blood supply, from operative trauma, but by exerting traction on the free ends of the strip, the ureter is pulled away from the wall of the bladder, exposing the field for the next procedure (Fig. 1a). The wall of the bladder is then incised with the belly of a scalpel until the mucosa is exposed in such fashion as to outline a rosette of the wall of the bladder, into which both the ureter and vesical artery enter (Fig. 1b). When this area is properly delimited the mucosa is cut through, especial care being taken to bisect the trigone so as to avoid encroaching on the opposite orifice (Fig. 2a). At all times the relation of the blood supply to the segment must be borne in mind, for on its preservation depends the success of the



operation. The bladder is then closed by means of two layers of inverting sutures (Fig. 2*b*) and the rosette of the wall of the bladder is carried through a median rectus stab wound without torsion and sutured to the skin after sufficient skin has been removed to accommodate the transplanted piece without tension (Fig. 2*c*). The abdominal wound is closed in layers.

It will be found helpful to insert ureteral catheters as soon as the bladder is opened and the orifices are identified. The transplantation of both ureters is done in essentially the same manner; the neck of the bladder is closed either by ligature or purse-string suture, and the two segments to be transplanted are trimmed on their fundic margins to get rid of the excess tissue, and then are transplanted as described.

The post-operative care is important. The animal must be inspected twice daily. The orifices must be kept free from uriniferous incrustations,

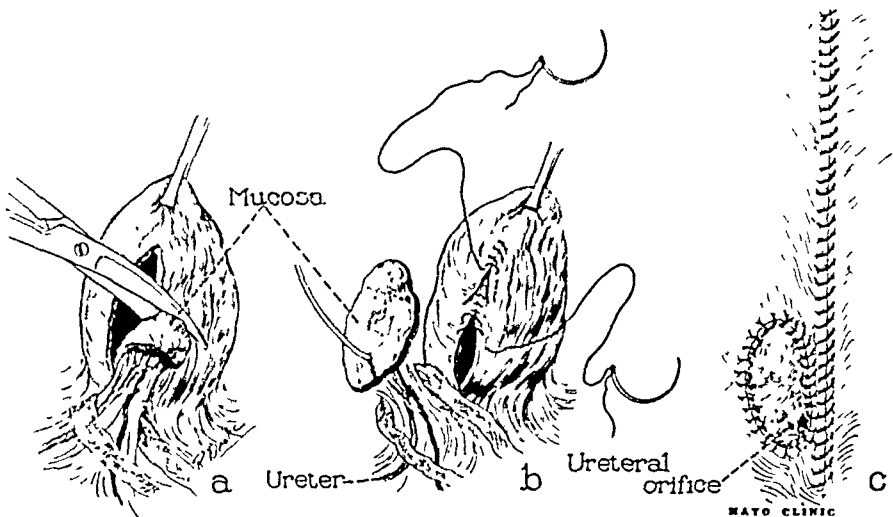


FIG. 2*a*.—Complete isolation of the ureter and accompanying blood-vessel and wall of bladder, *b*, repair of the opening in the bladder; and *c*, the completed transplantation.

and excoriation of the skin must be prevented. The frequent use of physiologic sodium chloride infusion will be found helpful in the resultant flushing of the urinary tract.

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## BOOK REVIEW

DIE AVERTINNARKOSE IN DER CHIRURGIE. BY PROFESSOR W. ANSCHUTZ, M.D., K. SPECHT, M.D., and FR. TIEMANN, M.D., 8vo; cloth; pp. 605. Julius Springer, Berlin, 1930.

The authors have gathered together various data relative to the administration of avertin as an anæsthetic since its discovery by Eichholtz, in 1926, and its first administration rectally by Eckstein of Düsseldorf. The general deduction is that it is unsafe to induce full narcosis with it but that used as a general basic anæsthetic, its exhibition is most satisfactory. The results of several thousand cases are analyzed.

The substance is a tribromomethyl alcohol. It is to be administered in dosage according to the patient's weight, the average being 100 milligrams per kilogram. The dosage will be varied, however, according to the experience of the administrator. Thus, children and young adults will require relatively larger doses than the aged. Obese and debilitated patients and those in whom there is an impaired elimination should also receive smaller dosage.

Its use is contraindicated in instances of severe kidney and liver derangements, in cases of marked arterial hypertension and in cachexia, shock, acidosis and diabetes.

The method of administration of avertin is most simple. The tribromomethyl alcohol is a heavy fluid. The amount elected to be used, usually between 4 and 5 cubic centimetres, is added to distilled water previously heated to 105° Fahrenheit. If the mixture is cooler, the avertin will crystallize. This is then shaken until the drug is thoroughly admixed with the distilled water. The resultant solution is then tested with congo red for assurance that there is no free bromine present which would prove irritating to the rectal mucosa. The mixture is introduced into the lower rectum through a funnel and small rectal tube or syringe. Details of its use by different surgeons such as Nordmann, Kreuter, Butzengeiger, Kohler, B. Martin, Els and Jager, and its use in children by Sievers, are given fully. If greater relaxation is desired, supplemental anæsthesia with ether or gas-oxygen may be employed or local anæsthesia induced. All three of these methods have been employed by the reviewer most successfully.

The patient falls asleep quite naturally in from four to ten minutes usually, the pulse and blood-pressure seldom showing noticeable alteration, the breathing becoming possibly a little more shallow and the face a trifle flushed. Usually, at the end of twenty minutes, the operative work may be proceeded with subsequent to which the patient sleeps normally for five to eight hours, a complete amnesia having been developed during the interim. There is seldom any nausea or vomiting and no period of excitement during

either induction or recovery. These aspects of avertin anæsthesia certainly are most desirable and of great importance in justifying its clinical use.

The 103 deaths which have been recorded are not, it would seem, a proper indictment against it as they were, in general, in instances of poor surgical risks and either the result of the employment of an hydrolyzed solution or had received an overdosage. Twelve only can be ascribed to an idiosyncrasy to the drug. From statistics, it would appear to be at least twice as safe as ether and five times safer than either chloroform or spinal anæsthesia.

It appears to be chiefly indicated in elderly people and in children. It has been most satisfactorily employed in severely wounded patients—in moving or undressing them, during direct or X-ray examination, at dressings or during manipulation of fractures. Excellent results have been obtained by its exhibition in tetanus and eclampsia. It lends itself particularly to operations of the head, neck or breast and is ideal in thyroid surgery.

From their experience, the authors conclude that the action of avertin is primarily that of a somatic sedative and not a cerebral sedative, and, as they aptly quote, "*Psychische Schonung ist gut, somatische Schonung ist besser!*" Thus it would seem that its effects might be enhanced by scopolamine or some barbituric acid derivative as an adjuvant.

The efforts of the authors to place the consideration of the question of rectal anæsthesia by use of tribromethyl alcohol (avertin) on a sound basis through this publication of their experiences and those of other is quite justified and indicates that we have added to the present well-recognized list of anæsthetic drugs another which comes nearest to giving the profession an easily administrable agent which will cause a perfect induction of anæsthesia, without excitement, without preliminary preparation or pre-operative medication and whose post-operative sequelæ are minimal.

The place of avertin is essentially that of a basic anæsthetic—full narcosis should not be attempted as that degree is dangerous. The supplemental use of gas, ether or novocain combines, to the highest degree, excellence and safety in anæsthesia, if it is remembered that carelessness will cause not only morbidity but mortality and that its administration should be superintended by a competent observer and anæsthetist.

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# ANNALS *of* SURGERY

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## ELECTROCAUTERIZATION IN THE TREATMENT OF HUMAN BITES\*

BY WILLIAM BATES, M.D.

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IN THIS study of human bites are grouped, not only bites originating as bites, but also wounds in the region of knuckles caused by blows against the teeth in fighting. The mouth contains more dangerous organisms than any other portal of the body. A wound caused by a tooth is infected immediately with many organisms of varying degrees of virulence. In addition, the infection is planted on the fertile soil of crushed tissue.

In the absence of rabies, infection of the wound is not to be expected in dog bites. A dog bite may be mutilating, and thus dangerous to life, or it may cause actual rabies, but only rarely does it cause infection.

I have treated many dog bites without cauterization. The wounds are thoroughly cleansed and a simple antiseptic applied without fear of resulting infection, thus confirming the adage, "As clean as a hound's tooth."

The infection in animal bites in general is not as severe as in a human bite. A horse bite is more of a pinch than a bite and seldom breaks the skin. A cat bite produces a wound that soon shows severe infection. Such a wound is best treated as a human bite. If the skin is broken by either a horse or a cat bite, tetanus antitoxin should be administered.

In spite of the difference in bacteriology, and the progress of the resulting wounds, we originally attempted to treat the human bite the same as an animal bite, by phenol cauterization and the application of various antiseptics. Our results were bad.

Regardless of the type of treatment given at first, the proportion of human bite cases that became worse from day to day was entirely too great.

In going over the records of three dispensaries in which I have worked, I found in the past seven years that we have treated over two hundred cases of wounds infected from human teeth.

Various other forms of treatment advised in surgical literature gave equally unsatisfactory results. Papers have appeared occasionally in the form of case reports, three<sup>1, 2, 6</sup> of these reporting the similarity of infecting organisms, but of no help in treatment. Some articles<sup>2, 3, 4</sup> have detailed the bacteriologic studies in from one to six cases. The result of these studied cases has been to attribute the infection to the organisms of Vincent's angina. Another bacteriologic study<sup>5</sup> of a bite showed "Only ordinary staphylococci, no streptococci nor other malignant organisms."

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\* Read before the Philadelphia Academy of Surgery, November 3, 1930.

Investigations by Hennessy<sup>3</sup> and Peters<sup>4</sup> have shown that when *B. fusiformis* and its symbiotic spirochete recovered from their cases of human bites were injected into the peritoneal cavity of laboratory animals, they would not multiply and nothing happened; or at times, the injection produced only a very mild infection. The writers concluded that the trauma to the tissue by the teeth produced the factor necessary for reproduction and spread of the infection.

Bacteriologic reports in some of my own cases were taken before treatment was given. Unfortunately, I had no studies made at the time when we were seeing the late severely infected wounds. From these few reports, we learned that the *B. subtilis* was sometimes present, occasionally the streptococcus viridans was reported and usually the staphylococcus aureus and staphylococcus albus were present. In none of our cases studied from smear and culture taken prior to treatment did we find the organisms of Vincent's angina.

Prior to our instituting a change in therapy, the patients came to the dispensaries after a variety of first treatments, and in various stages of wound infection. As an example of first treatments, the figures from one accident ward in 1924 indicate—thirty-six cases were treated—one with incision and drainage, five with mercurochrome, fourteen with iodine, three with silver nitrate and thirteen with phenol and alcohol. The wounds soon showed evidence of foul infection. Usually they had a green sloughing edge, marked swelling about the point of injury, and a characteristic skatol-like odor. The patients complained bitterly of pain. Lymphangitis and lymphadenitis appeared shortly. It soon became necessary to give wide drainage, even in the cases in which incision and drainage were part of the first treatment.

Tendon slough and extension of infection up the tendon sheath were frequent. Often the whole hand became oedematous and later osteomyelitis of the phalanx or metacarpal developed. A bite wound penetrating to the phalanx frequently meant amputation of the finger. The dorsum of the hand, just proximal to the metacarpo-phalangeal joint is frequently pierced by a tooth in bare hand fighting. According to pugilistic style of the injured, these wounds are over the distal end of either the second or fifth metacarpal. Frequently the complete severance of the extensor tendon, and even fracture of the metacarpal results. Immediate tendon repair is contraindicated because of impending sloughing.

Delay in first treatment, or too great an interval between first and second treatment was frequently encountered. The original wound was often trivial and to the patient apparently unimportant. The delay in applying for treatment, or in some cases, a misleading history as to the cause of the wound, is commonly due to shame on the part of the patient. An attempt is sometimes made to cover up a fight and attribute the wound to an industrial accident. In one case, the patient attributed the wound to a dog bite. Pain finally draws them to the doctor for treatment. Yet, in all fairness to the patient, there was not enough difference between a neglected wound,

and one apparently well-cared-for under the old forms of treatment, to attribute the spreading of the infection to neglect. The condition of the wound was dependent on the virulence of the infection and the amount of crushed tissue present. In the finger cases, the osteomyelitis usually developed so rapidly that amputation was the rule rather than the exception.

Thus far the discussion has been limited to bites which cause a penetrating wound. The avulsive bite and the amputating bite are of less severity from an infection standpoint. These cases present a large open wound, freely drained, and all crushed tissue is on the surface.

Certain of the incomplete avulsive bites leave a double row of penetrating tooth marks, mainly on cheek, nose, lip, deltoid region or calf of leg. These wounds become quite troublesome as there is much crushed tissue and frequently the area between the rows of teeth marks has been deprived of its blood supply.

Because of the bad results obtained with the older forms of treatment, I started, in 1925, to treat human bites with the electric cautery. The technic is simple, and the apparatus is available in every hospital. The patient is given a gas anæsthesia as soon as permission can be obtained. A cautery knife or a post-cautery blade is heated to a cherry red. In the penetrating bite cases, the whole tooth mark is removed with the cautery. There is practically no bleeding and the nerve ends are destroyed by the heat. The wound is dressed with a mild antiseptic. The patient awakes with a pain-free wound. Subsequent dressing consists of boric-acid ointment, or mercurochrome or other mild antiseptic applications. The scar produced is much less than one resulting from a scalpel excision of the same size. In the avulsive and amputating bites, the entire raw surface is seared with the cautery. In the massive bite where avulsion failed, the question of treating as double penetrating wounds, or as avulsion, arises. The decision depends on the amount of intervening tissue and the condition of the blood supply. If doubt exists, the avulsion is completed, and the whole new surface is seared. The best time to apply this treatment is immediately after the wound is produced.

It has been claimed on theoretic grounds that the cautery should not be used when the infection has spread so widely that complete removal of all infected tissue is impossible, because sealing off the lymphatics will prevent free drainage. However, I have used the cautery on the third or fourth day in numerous cases, in some of which all the infected tissue could not be removed. These cases have had very satisfactory results because of the immediate destruction of the primary focus, drainage quickly reestablished into the newly created open wound and the normal phagocytic action is capable of destroying the organisms in the surrounding lymphatics.

We have treated over one hundred cases of human bites by electrocauterization, and extension of infection thereafter occurred in only one case in which the extensor tendon of an index finger was severed, with a fracture of the distal end of the second metacarpal extending into the joint, during

a fist fight. In spite of cauterization on the second day, amputation of the index finger and part of the metacarpal became necessary. With the exception of that case just detailed, and one other who, at first, attributed his bite to a dog and therefore was not treated by electrocauterization, we have not had to admit any human bite cases to the hospital since 1925. This contrasts most favorably with the long hospitalization, and multiple operative procedures found prior to 1925. We have never computed the hospital days required per patient in our early cases but cases reported by other writers give figures from forty-five to fifty-four days.

Wound healing is frequently complete by the fourteenth, and almost always before the twentieth day, when the original treatment consists of electrocauterization.

The comfort of the patient and the economic saving, both to the patient and to the hospital, amply justify the simple procedure of electrocauterization of human bites.

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# CIRCULATORY DISEASES OF THE LOWER EXTREMITIES

WITH SPECIAL REFERENCES TO TESTS OF CAPILLARY CIRCULATION\*

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CIRCULATORY imbalance between the arterial system of efferent vessels and the afferent vessels of the venous and lymphatic systems may produce a variety of symptoms. Clinically this is manifested by the cold, discolored leg of arteriosclerosis, the swollen and frequently ulcerated leg associated with varicose veins, and finally the brawny swelling of lymphœdema.

Pathologic changes in one or more of these systems may produce combined dysfunction. Lymphœdema, for example, often accompanies impairment in the venous return of an extremity as is seen in varicose veins or more especially thrombophlebitis. In this instance venous stasis is assigned the primary rôle, whereas in fact, obliteration of the lymphatic vessels is essentially responsible. That the integrity of the circulation is not interpreted to the clinical satisfaction of many is borne out by the numerous clinical methods advocated. A notable few are color changes in the extremity in different positions; testing the reaction time following partial and total occlusion of the femoral artery; observation of the hyperemic reaction after pressure, the recording of temperature in the extremity of tactile sense, thermometer, thermocouple and galvanometer; the use of the calorimeter of Stewart, the viscometer and the oscillometer of Panchon, blood-pressure estimations, röntgenograms following introduction into the vessels of opaque solutions and lastly the intracutaneous injection of saline and histamine acid phosphate with careful observation as to their characteristic reactions. It is with a comparison of the last-mentioned tests in a variety of circulatory disturbances that this paper particularly deals.

*The Intradermal Salt Test.*—Aldrich and McClure found that 0.2 cubic centimetres of an 0.85 per cent. solution injected into the skin of a normal individual required sixty minutes or more for complete absorption. In cases showing œdema or other evidences of circulatory insufficiency the disappearance time is decreased in direct ratio to the degree of œdema or anoxæmia produced by the vascular involvement.

Stearn has used this test in a number of vascular diseases of the lower extremities affirming that it is a simple, rapid and accurate method of determining circulatory deficiencies.

*The Histamine Test.*—Sir Thomas Lewis has shown that following the introduction of a minute amount of histamine into the skin there followed: First, local dilatation of capillaries, venules and arterioles by direct action (a purple spot); second, widespread dilatation of surrounding arterioles resulting from a local reflex (the flare); and third,

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\* Read before the Southern California Medical Association April 4 and 5, 1930.



local increased permeability of the wall of minute vessels by direct action (the wheal). Certain of his experiments show that, if the circulation is completely obstructed, neither wheal nor flare follows the introduction of histamine. Also if the skin is cooled by placing in water from 12° to 15° C., the development of wheals is much retarded, this being interpreted as the result of decreased blood-supply.

These experiments of Lewis suggested that the reaction might change similarly if pathologic change obstructed the circulation and so give useful evidence of diminished peripheral blood-flow and blood-pressure, especially in the extremities. One finds that in normal persons the reaction of the skin of the feet to histamine is prompt and complete; but in cases in which there is strong clinical evidence of deficient circulation the reaction is delayed, reduced or incomplete, and this may occur where the clinical examination is essentially negative.

Starr lists the abnormal reactions in relation to their importance as follows: (1) Delay in appearance of the reactions; (2) reduction in the intensity of the reaction; (3) failure of the flare or the wheal to appear, the site of puncture being marked only by the purple spot of capillary dilatation described by Lewis where the circulation was completely obstructed. If nothing appears at the site of puncture, an error in technic should be suspected.

The wheal is by far the most important part of the reaction. The flare is sometimes indefinite in outline and difficult to see, especially in anæmic patients.

Following his work on arteriosclerotic and diabetic patients, Starr concludes that the absence of histamine reactions means an arterial occlusion of some degree and advocated it as a test of circulation.

De Takats reports that of thirty patients with varicose veins, approximately 50 per cent. showed an abnormal reaction.

*Analysis of Cases.*—A total of eighty-nine cases was examined. This group included fifteen cases of normals in children, twelve cases of normals in adults, fifteen cases of varicose veins without ulceration, twenty cases of varicose ulcers, five cases of arteriosclerotic ulcers, five cases of traumatic ulcers, four cases of chronic ulceration following burns, two cases of luetic ulcers, two of diabetic ulcers, three cases of thrombophlebitis and six cases of œdema of the legs of cardiac origin.

The salt and histamine tests were performed on these extremities at levels of the ankle, mid-leg and mid-thigh.

For the convenience of comparison each was calculated on a percentage basis, so that the figures in accompanying charts represent percentage variations from normal. In the salt test 0.2 cubic centimetres of an 0.85 per cent. salt solution was injected with a hypodermic needle intracutaneously, a normal 100 per cent. reaction requiring sixty minutes or more for the absorption of the resulting wheal. For the histamine test a 1:1000 solution of histamine acid phosphate in physiologic solution of sodium chloride was applied with a medicine dropper to the skin and six or seven punctures with a fine hypodermic needle made. Observations were recorded at two-and-one-half-, five-, ten- and fifteen-minute intervals. A normal 100 per cent. response in this test was interpreted following the typical reaction (presence of both wheal and flare) in two and one-half minutes with its completion in five minutes. The greatest intensity was usually reached in from five to fifteen minutes.

# CIRCULATORY DISEASES LOWER LIMBS

CHART IA  
Normals—Children

| Age.....          | 7        | 5        | 11        | 6        | 10        | 13                | 6        | 11m                      | 8            | 4                | 4        | 4           | 12           | 8m           | 7                    |
|-------------------|----------|----------|-----------|----------|-----------|-------------------|----------|--------------------------|--------------|------------------|----------|-------------|--------------|--------------|----------------------|
| Diagnosis         | Pyelitis | Pyelitis | Pneumonia | Pyelitis | Pneumonia | Leutic Adenopathy | Pyelitis | Malnutrition Dehydration | Otitis Media | T. B. Meningitis | Pyelitis | Burns, Back | Otitis Media | Malnutrition | Tonsils and Adenoids |
| No. of cases..... | 1        | 2        | 3         | 4        | 5         | 6                 | 7        | 8                        | 9            | 10               | 11       | 12          | 13           | 14           | 15                   |
| Thigh.....        | 90       | 60       | 90        | 70       | 80        | 100               | 90       | 40                       | 80           | 60               | 70       | 90          | 60           | 100          | 70                   |
| Leg.....          | 90       | 60       | 90        | 70       | 80        | 100               | 90       | 40                       | 80           | 60               | 70       | 90          | 60           | 100          | 70                   |
| Ankle.....        | 90       | 60       | 90        | 70       | 80        | 100               | 90       | 40                       | 80           | 60               | 70       | 90          | 60           | 100          | 70                   |
| Histamine.....    | 100      | 70       | 50        | 90       | 100       | 100               | 75       | 90                       | 80           | 45               | 60       | 50          | 80           | 80           | 50                   |
| Control.....      | 100      | 100      | 80        | 100      | 80        | 100               | 95       | 90                       | 90           | 60               | 100      | 90          | 80           | 100          | 90                   |

Note definitely low salt values in Cases 2, 4, 8, 10, 11, 13, and 15, with corresponding low histamine values in most instances. Also abnormally low histamine values in Cases 3, 7, 10, 12, and 15. The low salt value in Case 8 is obvious in association with the abnormal water balance. There is more variation in these cases than would be expected in such a group showing no circulatory disease.

CHART IB  
Normals—Adults

|                   |     |    |    |     |     |     |    |     |     |    |     |    |
|-------------------|-----|----|----|-----|-----|-----|----|-----|-----|----|-----|----|
| Age.....          | 30  | 83 | 72 | 25  | 23  | 28  | 35 | 29  | 55  | 42 | 70  | 30 |
| No. of cases..... | 1   | 2  | 3  | 4   | 5   | 6   | 7  | 8   | 9   | 10 | 11  | 12 |
| Thigh.....        | 80  | 60 | 90 | 90  | 100 | 100 | 70 | 80  | 90  | 80 | 90  | 80 |
| Leg.....          | 80  | 65 | 90 | 95  | 100 | 100 | 60 | 80  | 90  | 80 | 90  | 70 |
| Ankle.....        | 80  | 65 | 90 | 95  | 100 | 100 | 60 | 80  | 90  | 80 | 90  | 70 |
| Histamine.....    | 90  | 80 | 90 | 80  | 100 | 100 | 60 | 60  | 75  | 70 | 95  | 85 |
| Control.....      | 100 | 90 | 95 | 100 | 100 | 100 | 90 | 100 | 100 | 90 | 100 | 90 |

Feeling that the group of children tabulated was not a fair index of normal reaction, twelve normal adults of varying ages were examined. In this group we obtained less variation, although Cases 9, 10, and 12 could be classed as definitely border-line, while 2 has a low salt value, 7 is below normal with both the histamine and salt, and 8 has a definitely low histamine.

CHART II  
Varicose Veins—No Ulcerations

| No. of case..... | 1  | 2  | 3  | 4  | 5   | 6   | 7  | 8  | 9   | 10 | 11  | 12 | 13  | 14 | 15 |
|------------------|----|----|----|----|-----|-----|----|----|-----|----|-----|----|-----|----|----|
| Thigh.....       | 70 | 80 | 85 | 90 | 80  | 60  | 90 | 60 | 80  | 70 | 60  | 90 | 60  | 80 | 90 |
| Leg.....         | 70 | 70 | 70 | 90 | 80  | 60  | 90 | 50 | 80  | 70 | 60  | 90 | 70  | 70 | 85 |
| Ankle.....       | 65 | 80 | 70 | 90 | 100 | 70  | 90 | 50 | 80  | 70 | 60  | 90 | 60  | 70 | 85 |
| Histamine.....   | 65 | 90 | 70 | 60 | 60  | 70  | 60 | 45 | 70  | 70 | 65  | 60 | 70  | 70 | 60 |
| Control.....     | 90 | 90 | 70 | 90 | 100 | 100 | 90 | 80 | 100 | 90 | 100 | 90 | 100 | 90 | 90 |

Note consistently low values in both tests in this group with greater uniformity in the histamine reaction.

CHART III  
Varicose Ulcers

| No. of case.... | 1   | 2  | 3  | 4   | 5   | 6  | 7   | 8   | 9  | 10  | 11  | 12  | 13 | 14 | 15  | 16  | 17 | 18 | 19  | 20 |
|-----------------|-----|----|----|-----|-----|----|-----|-----|----|-----|-----|-----|----|----|-----|-----|----|----|-----|----|
| Thigh.....      | 90  | 70 | 80 | 85  | 80  | 80 | 85  | 80  | 60 | 80  | 100 | 85  | 90 | 95 | 100 | 95  | 60 | 90 | 80  | 50 |
| Leg.....        | 85  | 70 | 75 | 85  | 70  | 90 | 80  | 80  | 60 | 80  | 100 | 85  | 90 | 95 | 100 | 90  | 60 | 90 | 80  | 40 |
| Ankle.....      | 85  | 70 | 50 | 85  | 65  | 90 | 80  | 80  | 60 | 80  | 90  | 70  | 90 | 80 | 100 | 90  | 60 | 90 | 80  | 40 |
| Histamine.....  | 100 | 80 | 80 | 100 | 75  | 95 | 100 | 60  | 75 | 65  | 75  | 65  | 80 | 90 | 50  | 60  | 55 | 60 | 75  | 70 |
| Control.....    | 100 | 90 | 90 | 100 | 100 | 95 | 100 | 100 | 70 | 100 | 100 | 100 | 90 | 95 | 100 | 100 | 90 | 95 | 100 | 90 |

# HOLDER AND McDOUGALL

Note generally higher values of saline tests in this group. With several exceptions there are proportionally lower and more consistent histamine values as in Chart II.

CHART IV

| No. of cases..... | Arteriosclerotic Ulcers |     |     |    |     | Traumatic Ulcers |    |     |    |     | Chronic Ulceration Following Burns |    |    |    |
|-------------------|-------------------------|-----|-----|----|-----|------------------|----|-----|----|-----|------------------------------------|----|----|----|
|                   | 1                       | 2   | 3   | 4  | 5   | 1                | 2  | 3   | 4  | 5   | 1                                  | 2  | 3  | 4  |
| Thigh.....        | 80                      | 60  | 80  | 95 | 70  | 80               | 80 | 90  | 80 | 60  | 80                                 | 60 | 70 | 80 |
| Leg.....          | 80                      | 60  | 75  | 95 | 70  | 80               | 70 | 90  | 80 | 50  | 60                                 | 60 | 70 | 70 |
| Ankle.....        | 80                      | 60  | 80  | 95 | 70  | 80               | 70 | 90  | 70 | 50  | 70                                 | 60 | 75 | 70 |
| Histamine.....    | 100                     | 90  | 50  | 75 | 100 | 80               | 80 | 80  | 75 | 60  | 50                                 | 60 | 45 | 80 |
| Control.....      | 100                     | 100 | 100 | 80 | 100 | 100              | 90 | 100 | 80 | 100 | 90                                 | 80 | 95 | 90 |

Due to the small number of cases in the arteriosclerotic group any pertinent deductions are not possible. Here the saline values run consistently lower while in three cases the histamine test was practically normal. In this instance we expected uniform low values with both tests.

Again in the traumatic group both tests were generally inconclusive, possibly the histamine reaction showing a more uniform downward trend.

In the chronic ulcerations following burns both tests showed consistently low values.

CHART V

| No. of cases..... | Luetic Ulcers |    | Diabetic Ulcers |    | Phlebitis of Extremity |     |     | Cardiac Œdema of Leg |     |    |     |     |     |
|-------------------|---------------|----|-----------------|----|------------------------|-----|-----|----------------------|-----|----|-----|-----|-----|
|                   | 1             | 2  | 1               | 2  | 1                      | 2   | 3   | 1                    | 2   | 3  | 4   | 5   | 6   |
| Thigh.....        | 90            | 70 | 45              | 50 | 90                     | 70  | 80  | 10                   | 15  | 35 | 20  | 30  | 20  |
| Leg.....          | 90            | 70 | 45              | 50 | 90                     | 70  | 80  | 10                   | 15  | 30 | 20  | 30  | 15  |
| Ankle.....        | 90            | 60 | 45              | 50 | 90                     | 60  | 75  | 10                   | 15  | 30 | 20  | 30  | 15  |
| Histamine.....    | 100           | 80 | 60              | 70 | 90                     | 100 | 60  | 75                   | 50  | 90 | 85  | 90  | 80  |
| Control.....      | 100           | 90 | 100             | 80 | 100                    | 100 | 100 | 100                  | 100 | 95 | 100 | 100 | 100 |

In the two cases of luetic ulcers no definite result was obtained except low salt values in one case.

In cases of diabetic ulcers both tests definitely recorded impaired circulation.

In thrombophlebitis one case showed a normal reaction to the salt test. Of the other two, one had a low salt value with a normal histamine, the other showing lowering of both, particularly the histamine.

The cases of cardiac œdema all showed very low values with the salt test. The histamine reaction was within normal variations in three instances and moderately lowered in two.

## COMMENT

We have tried to reduce the margin of error in estimating these results to a minimum. Of necessity, individual judgment must enter into the valuation of each case. Results have been recorded without regard to preconceived opinions. With this admission of a possible source of error we feel there is a large degree of uncertain variation in these tests, with little correlation between the two.

A general impression in this particular group of cases with circulatory disease is that the histamine test, although bearing the above general criticism, gives a better index of possible circulatory insufficiency than the salt test.

# DERANGEMENTS OF THE SEMILUNAR CARTILAGES

BASED ON A STUDY OF 388 OPERATIVE CASES

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FROM THE MACAUSLAND ORTHOPEDIC CLINICS

IN AMERICAN medical literature there is a noticeable lack of contributions devoted to derangements of the semilunar cartilages. To be sure, the general field of internal derangements of the knee-joint, embracing pathology of the semilunar cartilages, fat-pads, synovial membrane, and the joint surfaces with their ligamentous structures, has been discussed in numerous articles, but the reports pertaining to the menisci have been comparatively few. This paucity of data gave me the incentive to compile the derangements that had been treated in our clinics. From 1910 until the present time the operative cases have numbered nearly 400. The purpose of this article is to present a study of derangements based upon this series of cases, and to correlate the clinical findings, the pathology, and the end-results.

In this study I have been greatly impressed with the frequent occurrence of errors in diagnosis and treatment of mild joint injuries. There seems to be a tendency on the part of many physicians to regard a slight damage to the meniscus as too trivial for treatment. As a result, the joint is left in a weakened condition, exposing it to the development of further symptoms that may become a potential danger to the function of the joint. In this paper, particular emphasis will be placed upon the recognition and treatment of mild injuries.

1. *Anatomical Considerations.*—The great strength of the knee-joint lies, not in its osseous structures, but in its supporting ligaments and muscles.

2. A relationship exists between the internal semilunar cartilage and the internal lateral ligament, a relationship that does not exist between the external semilunar cartilage and the external lateral ligament. Most anatomists are of the opinion that the external surface of the internal semilunar cartilage is firmly connected with the inner lateral ligament, making the two dependent upon each other in movement. Fisher<sup>1</sup> in his work found that only the posterior fibres of the ligament were firmly attached to the peripheral border of the semilunar cartilage, while the anterior part was loosely connected. Thus, a weak mechanical spot exists between the fixed and the mobile parts of the cartilage.

3. The internal semilunar cartilage is firmly attached along its entire border to the capsule.

4. The external semilunar cartilage is more mobile than the internal. There is no connection with the lateral ligament and it is less closely adherent to the articular capsule. Also, its attachments are more lax, and the cartilage moves as a whole.

5. A possible connection between injuries of the crucial ligaments and lesions of the semilunar cartilages is suggested by Galeazzi.<sup>3</sup>

6. Fisher<sup>1</sup> mentions the possibility of confusing an injury to the semilunar cartilage proper with a lesion of the semilunar extension of the infrapatellar fat-pad.

7. At the completion of the movement of extension, and at the beginning of flexion, some rotation takes place, a screw-like motion, which locks or unlocks the joint.

*Etiology.*—There are several factors that may predispose injury to the cartilage. An individual whose ligamentous and capsular structures are in a lax condition as the result of an occupational strain or synovial effusion is more susceptible to cartilage injury. (It is strange, however, that healthy persons whose ligaments and muscles are in perfect tone are affected more often.) Static disturbances due to flat or pronated feet, or due to knock-knee that leads to the stretching of the inner section of the capsule and the internal lateral ligament, are potential factors. Some individuals may have cartilages with weak attachments, or the muscles and tendons surrounding the joint may not be in good tone.

The immediate etiological factor in the majority of cases is trauma. When one considers that the knee-joint is relatively unprotected by soft parts, and when one considers that the joint acts as a fulcrum for the two longest levers of the body, it seems remarkable that injury is not more common. By far the greater number of derangements is due to indirect trauma, as might be expected in view of the tremendous strain upon the ligaments and articular surfaces, amounting, if calculated, to thousands of pounds. The most common type of injury is a wrench or inward twist of the femur when the knee is flexed, the leg abducted, and the foot in a fixed position. Such a movement is often made in dodging or running, or in rising suddenly from a squat position. Consequently, trauma is frequent among workers, and among athletes who engage in strenuous forms of exercise. In reports by British operators, attention is called to the frequency of the lesion among miners, who, in rising from the squat position to throw a shovelful of coal over the shoulder, may suddenly twist the thigh. In the case of miners, the loss of tone in the muscles and ligaments as the result of working in a stooped position is a predisposing factor. This prevalence of the lesion among miners has led to the use of the term "miners' disease." Martin,<sup>4</sup> in a series of cartilage cases, noted the following distribution of injuries:

62.8 per cent.—miners

18.0 per cent.—football players

2.0 per cent.—athletes of some nature

In the series of cases which I am reporting, falls were responsible for the majority of the derangements. There was a high incidence among participants in sports, particularly football. Many other forms of games were



FIG 1—Fractured semilunar cartilage with complete detachment except at the posterior end

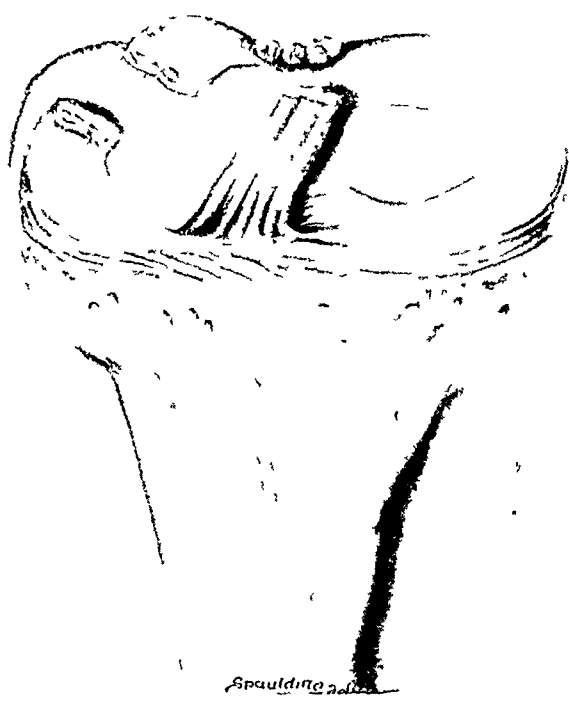


FIG 2—Transverse fracture of the cartilage.



FIG 3—Longitudinal tear with detachment of both extremities.



FIG. 4—Longitudinal tear in the semilunar cartilage.

represented, including hockey, baseball, basketball, tennis, polo, and wrestling. A certain proportion of the derangements was due to automobile accidents.

The primary injury in many cases is mild, resulting simply in a tearing or loosening of the cartilage. In such cases, the disability is usually slight. The treatment of these mild injuries should not be neglected, however, for once derangement has taken place, recurrence with acute symptoms is common.

*Direct trauma* may also be the cause of derangement of the cartilage, although this origin is much less common. As a rule, cartilage lesions due to direct injury are associated with severe trauma, such as fracture of the patella or tibial tuberosities, or rupture of the crucial ligaments. Occasionally, the cartilage may become jammed as the result of a blow on the inner side of the knee when the joint is flexed. The mechanism of such a derangement is as follows: When the blow hits the knee, it produces extreme abduction of the leg, and the individual, to prevent himself from falling, rises suddenly, thereby rotating the femur inward. (See Section on Mechanism of Injury.)

*Disease* of either a subacute or chronic nature may eventually lead to a derangement of the cartilage. The symptoms in these cases are often obscure, and the diagnosis is made only by a careful study of the history and after repeated detailed examinations. Local signs and symptoms of slow onset, but increasing in severity, in a case in which there is no history showing of trauma, should be regarded with caution. Not infrequently, when excision of the knee-joint is done in an adult case of tuberculous bone-disease, little or no meniscus is found, showing that cartilage changes take place early in such cases. In one of my cases with a predominance of cartilage signs, an exploratory operation revealed a loose internal cartilage with considerable capsular and synovial thickening. A piece of this infiltrated tissue was removed and, on pathological examination, was found to be tuberculous. Later, the knee went through the typical course of a tuberculous knee.

Arthritis of both the hypertrophic type and the infectious type has been demonstrated as the underlying cause of cartilage hypermobility in some of our cases. When infection of an arthritic nature is present, the cartilage undergoes changes that predispose it to injury. Pathological changes have been noted especially in the infectious destructive type in which there is an extravasation of fluid and detritus in the knee-joint.

*Age, Sex, and Joint-involvement.*—Derangements of the cartilage are most common in young people, that is, individuals between the ages of twenty-one and thirty. Injuries do occur later in life as well as before adolescence, but these cases are rarer. The age distribution in my reported series ranged from eight to sixty-six years. The majority of the patients were between the ages of twenty-one and thirty, the period in life when an individual is most active and at the height of his physical development. The ages between eleven and twenty years were next in frequency of occurrence.

The injury is much more common among men than women, a predominance that one expects to find in view of man's participation in athletics and in the more dangerous occupations. In the reported series, approximately 65 per cent. of the cases were males. Other operators have reported about the same proportion in their series.

The joints affected are usually about evenly distributed between the right and left. In our series there was only one more case of involvement of the left knee than of the right.

*The Frequency of Involvement of the Internal Cartilage.*—Lesions of the internal semilunar cartilage are more common than injuries of the external. In Martin's<sup>4</sup> series of 449 cases, 92 per cent. were injuries of the inner cartilage. In Henderson's<sup>5</sup> series of ninety-eight cases, ninety-four were lesions of the internal meniscus. In our series, 79 per cent. were injuries of the internal cartilage. Several explanations of the greater frequency of derangements of the internal cartilage have been advanced. There are, of course, the anatomical variations in the two menisci. The internal cartilage bears a certain relation to the internal lateral ligament and is firmly attached along its entire border to the capsule, whereas the external semilunar has no connection with the external lateral ligament and is much less adherent at its periphery. Consequently, the external cartilage is a more adaptable and mobile structure. Again, due to the weakness of the attachment of the anterior cornu of the internal cartilage, it is easily detached or split when there is a strain on the internal lateral ligament. There is also the possibility that the greater range of internal rotation of the femur, owing to the shape and size of the internal femoral condyle, plays a part in injuries to the internal semilunar. Another explanation is suggested in the accentuation of the direction of the line of force through the inner side of the knee when the foot is abducted, thus throwing a strain upon the internal semilunar cartilage. Galeazzi,<sup>3</sup> recognizing a close relationship between the crucial ligaments and the menisci, claims that the preponderance of internal cartilage lesions is due to the fact that in inward rotation of the joint the anterior crucial ligament bears the brunt of the stretching. Surls and Osgood<sup>6</sup> account for the frequency on a physiological basis, explaining that an individual, to maintain his balance in turning suddenly, twists inward and throws the weight on the other leg. It would naturally be awkward to turn outward and swing the free leg over the other.

When injury is direct, the prominence of the inner part of the knee, as well as the manner in which an individual maintains his balance, described above by Surls and Osgood, may account for the more frequent internal cartilage injuries.

*The Mechanism of Derangement.*—An explanation of the mode of production of injuries to the semilunar cartilages must be based upon clinical observations and experimental data. The effect of active motion in actual life must, of course, be taken into consideration in weighing the experimental



evidence. Several theories on the mechanism have been advanced. I shall refer to only the most probable ones.

It is agreed, in general, that sudden inward rotation of the femur upon a fixed tibia, with the knee in the position of flexion and the foot abducted, is the important factor in derangement. Most operators also agree that the internal lateral ligament plays an important rôle in derangements of the internal cartilage. This ligament, together with the muscles, resists any separation of the inner femoral condyle and its articulating area on the tibia, which might take place when the knee is in normal extension or slight flexion. Stretching or rupture of the ligament may occur when, with the foot fixed in the position of abduction and the knee slightly flexed, there is a sudden twisting movement by which the body weight is put on the joint and the femur rotated. The relaxation of the ligament causes the tibial surface and the internal femoral condyle to separate, allowing the cartilage to slip into the joint. Then, as the articular surfaces resume their normal position, the cartilage is nipped or jammed. Usually, it is the anterior half of the cartilage that is damaged when the femoral condyle rolls down on it.

Fisher<sup>1</sup> offers another theory on the mechanism. It is his opinion that the tenacity of the internal lateral ligament, and not the relaxation of this structure, is responsible for many injuries. In some instances, when the femur is rotated suddenly inward, the ligament remains intact, thus forming a hinge between the mobile anterior part of the cartilage and the fixed posterior part to which the ligament is attached. As a result, the anterior part of the cartilage may enter the joint, and, upon extension, become nipped, or the anterior or coronary attachments of the cartilage may be ruptured, or tears may occur opposite the fixed posterior part of the cartilage.

Galeazzi,<sup>3</sup> from his clinical observations and experimental work, concluded that lesions of the semilunar cartilage are more often associated with rupture of the crucial ligaments than is generally believed. It is his opinion that the semilunar cartilages and the crucial ligaments form one functional unit, and that the crucials are put under tension and resist rotation when the knee is in semiflexion. Tension on various parts of the crucial ligaments leads to injury of certain parts of the semilunar cartilages.

The mechanism of injuries of the external semilunar cartilage has not been studied so carefully as that of derangements of the internal cartilage. Fisher<sup>1</sup> advances the following explanation: The anterior horn of the external semilunar may be displaced when, with the knee in the position of flexion, the femur is rotated externally upon a fixed tibia, or when the tibia is rotated internally upon a fixed femur. The posterior horn may be displaced when the femur is rotated internally upon a fixed tibia following or combined with extreme flexion.

*Surgical Pathology.*—There is a wide variation in the pathology of the cartilages. The types of injuries that it has been possible to determine may be classified as follows:

## DERANGEMENTS OF THE SEMILUNAR CARTILAGES

- (1) Hypermobile cartilage
- (2) Fractured cartilage
  - (a) Type
    - longitudinal
    - transverse or oblique
    - combination of transverse and longitudinal
    - bucket-handle
  - (b) Site
    - anterior end
    - posterior end
    - middle part
    - periphery
- (3) Totally avulsed cartilage
- (4) Fractures and dislocations
- (5) Cysts

Some of the various types of cartilage fractures found upon opening the joint are illustrated in Figs. 1, 2, 3, 4 and 5.

Attempts have been made to designate the relative frequency of each injury, but such a classification is almost impossible. In Martin's<sup>4</sup> series, definite fractures predominated; in Fisher's<sup>1</sup> series, the longitudinal fractures held first place, and detachment of the anterior horn and obvious fracture were next in frequency. In our series, the hypermobile cartilage held a prominent place. There is a possibility that the hypermobile meniscus occupies the most prominent place in cartilage pathology, but owing to the mildness of the symptoms following a slight lesion, the joint does not come to operation until a later injury produces more extreme pathology. In severe injuries, the bucket-handle type of fracture is most commonly seen (Fig. 6).

In addition to the specific injury, the cartilage may be atrophied, thickened, calcified, fibrous or nodular. In some cases, it is difficult to discern the cartilage, so changed is its structure, while in other joints there may be no trace of the meniscus. Loose bodies due to the breaking away of parts of the cartilage may be present. Occasionally, a case is seen in which the cartilage has an apparently normal appearance. Henderson,<sup>5</sup> in recording ninety-eight cases of cartilage derangement, mentioned eighteen instances in which, except for a slight mobility of the capsule, there was no appreciable change despite the presence of the usual symptoms.

The true pathology does not always coincide with the symptoms, that is, intermittent attacks following a fractured cartilage may be mild, whereas a simple hypermobile cartilage may cause severe symptoms. Occasionally, the symptoms may indicate an injury of the internal cartilage, but upon exploration this meniscus is found in perfect condition, and the external cartilage, on the contrary, is deranged. In a certain proportion of cases, the symptoms are somewhat indicative of the pathology. For instance, a sense of weakness

is the predominating symptom in the presence of the hypermobile type of cartilage or in cases of loosening of an extremity. In detachments of the cartilage, slipping and sudden insecurity are the predominating signs.

*The Hypermobile Cartilage.*—The hypermobile cartilage may be an entity in itself, although it is possible that in many of these cases a marginal fracture exists, but is not observed. The abnormal mobility of the cartilage is the result of a slight injury that loosens the meniscus from its peripheral attachments. If dislocation takes place, the cartilage usually moves toward the

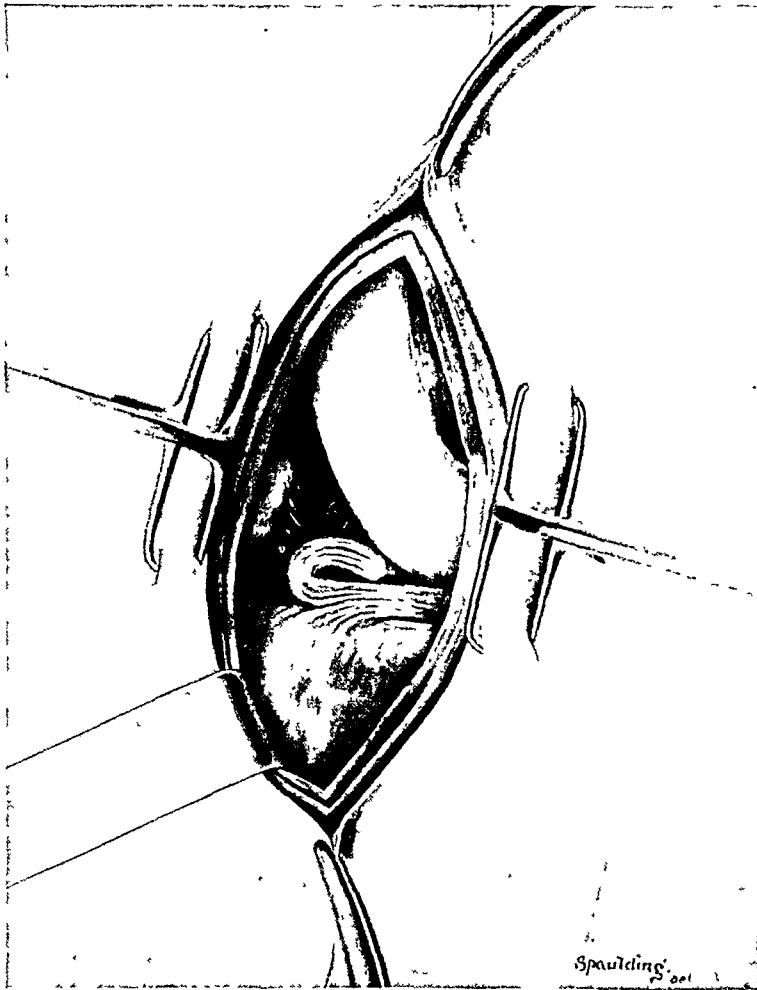


FIG. 5.—Detachment and folding over of the anterior end of the semilunar cartilage. Note the white, shining surface of the internal condyle and the top of the tibia.

centre of the joint, although, occasionally, a luxation toward the periphery is seen. The hypermobile cartilage is common among young girls, occurring as the result of a twist or wrench without history of further injury. The symptoms following the initial trauma are mild, and usually there is no locking of the joint. In this type it is particularly important to immobilize the knee-joint to provide an opportunity for repair; otherwise, the slight hypermobility may be the beginning of more extensive pathology in the

knee. If treatment is neglected, as often happens because the patient is not seriously disabled, recovery takes place with the cartilage in a loosened condition. A subsequent injury or slipping causes increased hypermobility and the cartilage may be caught between the articular surfaces. With each recurrent slip or pinch, the cartilage swells, thereby becoming more susceptible to further pathology. Total avulsion is not unknown in these cases.

In long-standing cases of a hypermobile cartilage, there are definite evidences of continued local irritation due to the constant rubbing of the meniscus. Villous changes may be felt in the capsule, the edges of the femur may be thinner, sharper, and flatter than normal, or actual hypertrophic changes may be present throughout the entire knee. The following case is one in which such changes were present.

CASE I.—L. L., aged fifty years, was injured twenty-five years previously while playing football in college. From that time the knee had been weak and frequently gave way when walking on uneven surfaces. During the last five years of disability the symptoms had increased.

The knee contained some fluid and was larger than the other knee. All the bony landmarks were prominent, and there was considerable crepitation on movement. The internal cartilage was felt to be large and swollen, and it snapped back and forth in flexion and extension. There were definite hypertrophic changes throughout the entire knee.

An exploratory operation was performed, and the cartilage removed. It was partly torn anteriorly and the remaining part was hypermobile and swollen. The margin of the joint-cartilage was hypertrophic, the articular surfaces were flattened, and the infrapatellar pad was increased in size.

The functional result was fair. The knee no longer slipped and gave way, but the general weakness continued because of the coexistent arthritic changes.

*Fractures.*—A fracture, tear, or split of the cartilage is a common lesion. It may be longitudinal, transverse or oblique, a combination of the longitudinal and transverse, or the so-called bucket-handle fracture. The tear may occur in the anterior end, the posterior end, the middle part, or along the margin of the cartilage. When the meniscus is torn loose at one of its attachments or when it is torn across, one fragment dislocates. In old-standing luxations the torn ends of the cartilage may become atrophied, or, in an occasional case, thinned.

The split occurs more frequently in the anterior part of the cartilage than elsewhere. If the peripheral attachment is also ruptured, it is not unusual to find a part of the inner edge of the anterior extremity of the cartilage projecting as a tag toward the centre of the joint. The cartilage is usually displaced inward, leaving a noticeable gap, which can be felt on palpation. Only rarely does the anterior tip displace outward or buckle backward, as shown in the accompanying illustration (Fig. 5). The tear is followed by symptoms of "catching" or "giving way," even if the cartilage still remains attached at its middle part. The normal cartilage thrust cannot be felt upon examination.

An isolated fracture of the posterior end is rare. It may occur in con-

nection with actual separation of the mid-portion of the cartilage or in total avulsion of the meniscus. Fisher,<sup>1</sup> in his description of the production of a posterior split or displacement, refers to Lang's theory. The latter is of the opinion that during forcible external rotation of the femur upon a fixed tibia, combined with flexion, the posterior part of the internal condyle sweeps across the posterior end of the cartilage, and if the flexion is extreme, the semilunar may be split or detached. Tenney<sup>2</sup> has shown that, in forcible abduction of the leg, the upper attachments of the internal lateral ligament may be ruptured, and the posterior part of the internal condyle slip over the posterior end of the semilunar and roll up the cartilage.

I have seen only one case—a fracture of the posterior third—in which a tear of the posterior end was demonstrable with practically no evident changes in the rest of the cartilage.

The patient was a man, twenty-two years of age, who, while playing basketball, felt something slip on the inner side of the left knee, and fell. The knee swelled considerably. From that time complete extension or flexion was impossible. During the following two months, the knee slipped out seven or eight times.

About fifteen months after the first attack, the knee was opened and the cartilage removed. A part of the cartilage at the junction of the middle and posterior thirds was entirely free. At this point the attachment of the cartilage to the ligament could not be removed, but since the strip was very narrow; it did not seem that it would cause trouble if allowed to remain in the joint. At the anterior tip the cartilage was broad and slightly thickened.

Examination six months after operation showed the knee to be in satisfactory condition. The strength and function were rapidly returning to normal. The patient wrote six years after the operation that he was satisfied with the result.

Fractures of the middle section of the cartilage are not uncommon. In such cases the cartilage often folds over on itself, bringing the razor edge away from the crucials. There is always a definite history of slipping, followed by almost total disability, and, in case of displacement, by flexion deformity. In the following case of a tear of this nature, the patient experienced such severe symptoms that she fell two or three times a day for a period of more than two years.

A girl, seventeen years of age, attempting to rise from the floor with the legs crossed, felt the knee lock, and could not straighten her leg. Fluid remained in the joint for two weeks. A second attack occurred a few months later. The knee was actually locked only twice more throughout the long period of disability, but the joint gave way frequently, sometimes as often as two or three times a day. Finally, the cartilage was removed according to the regular technic. The internal meniscus was found fractured in its middle part. The external cartilage was also excised as its posterior part was displaced and its anterior tip traumatized. The result was a perfect functional knee with full strength.

*Marginal Tears.*—It is possible that marginal splits are more frequent than is generally supposed, as they are easily overlooked, particularly in the hypermobile type of cartilage. In an occasional case, an incomplete transverse fracture, often combined with a longitudinal tear, may occur near the

periphery of the cartilage. Isolated longitudinal splits also may be found along the border of the disc.

*Types of Fractures.*—*The Longitudinal Fracture.*—Longitudinal fractures may occur in any part of the cartilage, or they may involve its entire length. The usual site of these fractures is about the junction of the anterior and middle thirds. The tear may be single or multiple, or it may be combined with a transverse fracture, thus producing a pedicled tag. In many cases the fracture occurs in a somewhat oblique rather than a true vertical plane. Strain upon the peripheral attachments is probably responsible for these longitudinal splits. Surls and Osgood<sup>6</sup> offer the explanation that a longitudinal fracture is probably the result of secondary damage to a cartilage already in a relaxed condition as the result of a previous trauma. The

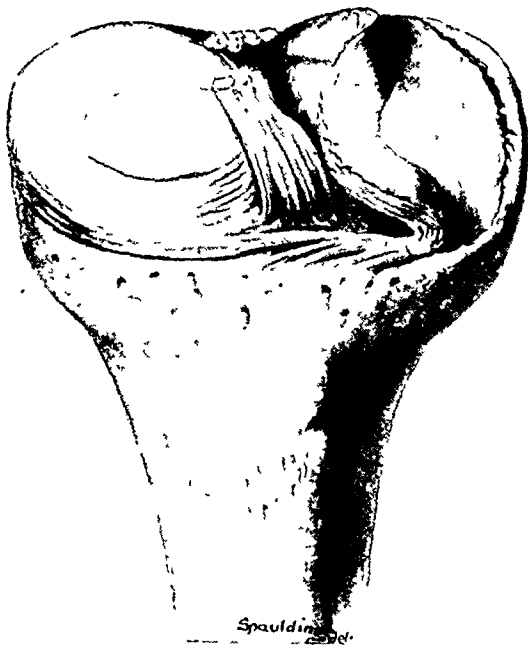


FIG. 6.—The "bucket-handle" type of fracture, showing the cartilage folded over in the intercondylar region.

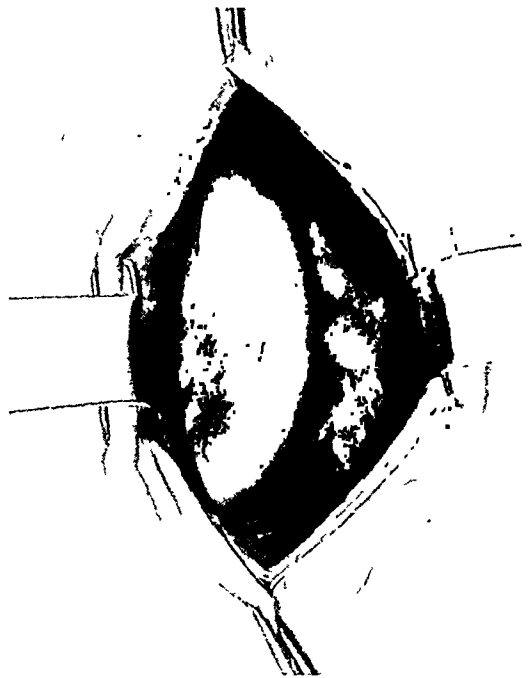


FIG. 7.—Loose internal semilunar cartilage, showing hypertrophic subpatella lipoma.

cartilage gets caught between the bony surfaces, there is a pull on the peripheral margin, and the pressure of the femoral trochlea holds the cartilage firm. The result is a long split near the anterior extremity of the meniscus. Wilson and Cochrane<sup>7</sup> call attention to the occurrence of a longitudinal fracture in the middle part of the cartilage when its anterior end is snapped, but without the attachment giving way and with the peripheral attachments remaining intact. When the small inner crescent formed by the longitudinal tear swings in between the condyles, the fracture is called the bucket-handle type (Fig. 6).

*The Transverse and Oblique Fracture.*—According to Fisher's<sup>1</sup> observations, the common site of these fractures is the level of the posterior fibres of the internal lateral ligament. Fisher finds that the oblique and incomplete fracture occurs most frequently with the fissure running horizontally only

part way through the cartilage so that the fragments move upon each other. Wilson and Cochrane<sup>7</sup> believe that the cartilage is likely to be torn across when a part of the anterior extremity of the cartilage gets caught in the intercondylar notch and the peripheral attachments remain intact. If the fracture is complete, the anterior fragment may become entirely detached and form a loose body. In other cases, the anterior half of the cartilage, being abnormally mobile, may become caught between the joint surfaces with resulting locking of the joint. Fisher<sup>1</sup> has emphasized the importance of careful inspection of the cartilage to detect these fractures, for when the meniscus is viewed from above, it may appear normal owing to the obliquity of the tear.

*The Bucket-handle Fracture.*—(Fig. 6.) A type of fracture seen frequently in severe injuries is the so-called bucket-handle tear. This is a longitudinal split in which a loop of the cartilage becomes detached and enters the intercondylar notch, resembling the handle of a bucket. The production of these longitudinal fractures has already been explained under "The Longitudinal Fracture." The bucket-handle type of tear also occurs when, with the knee partly flexed and the foot rotated outward and abducted, sudden extension causes the condyle of the femur to jam down on the cartilage at about the junction of its anterior and middle thirds. The section detached enters the intercondylar notch.

*The Totally Avulsed Cartilage.*—A complete tearing of the cartilage from its attachments is not common. It is produced only by a very severe trauma.

*Associated Pathology.—Early Changes.*—Immediately following the injury there is extravasation of synovial fluid, which gradually grows thicker and more stringy. Free blood is present in the joint. The displaced meniscus always causes a synovitis.

*Later Changes.*—The synovial membrane becomes more fibrotic with each attack. The capsular ligaments are thickened as in any chronic joint process. There is usually atrophy of the quadriceps group. Wallace and Permar,<sup>8</sup> who made a careful study of the pathology in seventy-one cases of derangements in which arthrotomies had been performed, found proliferative inflammatory changes in the synovial membrane, which had given rise to pannus or a granulation tissue over the articular cartilage. In long-standing cases this cartilage had become eroded or even destroyed under the heavy pannus. Wallace and Permar also found that microscopically there was marked thickening of the connective tissue, with a large increase in the size and number of the small vessels, especially the capillaries. As to the fluid, there were quantities present in old-standing cases, of a serous, yellow, brown, or bloody character. Further, the fat pads showed much congestion, thickening, and induration. The fat tissue was compressed and atrophic as the result of marked fibrosis. In chronic cases the infrapatellar fat pad was enlarged, œdematous, and hæmorrhagic (Fig. 9).

Occasionally one sees small villi and fatty tabs attached to the menisci

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anteriorly. These tabs seem to be parts of the cartilage which have been stripped off, but not totally detached, and which have become hypertrophied. Pinching of these tabs causes sudden pain. If any bone or ligamentous damage was associated with the original injury, loose bodies may be found.

Not infrequently an arthritic process is associated with the deranged meniscus. The presence of a local hypertrophic arthritis in one knee-joint following a history of trauma suggests a cartilage injury. Hypertrophic changes take place at the point of irritation and are recognized by the prominent ridges, thinned cartilage on the bony surfaces, and a flattened appearance of the condyles and tibial tuberosities. Occasionally the changes

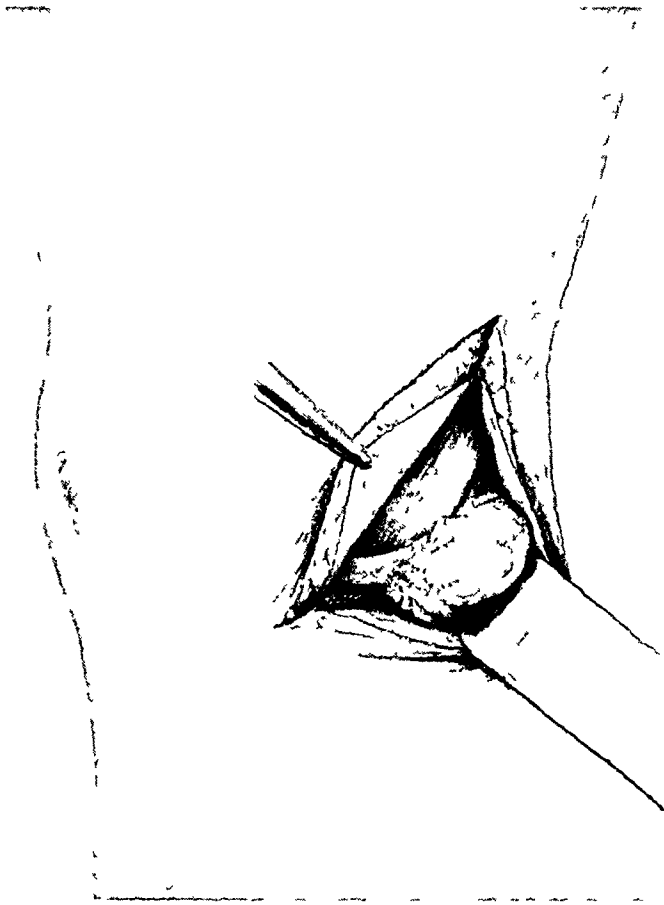


FIG 8—Cyst of the semilunar cartilage

are associated with loose bodies and hypertrophic fringes. These changes may become so marked that joint symptoms persist even after the removal of the cartilage.

*Cysts of the Semilunar Cartilages.* (Fig. 8.)—Since the year 1904 when this lesion was first described by Ebner,<sup>9</sup> practically all contributions on the subject have opened with a statement calling attention to the rarity of the lesion. From a careful survey of the literature, I should conclude that these cysts are far more common than is generally estimated. The total number of cases reported from 1904 to June, 1929, in so far as I have been able to ascertain, amounted to eighty-nine. This total is at considerable variance with the list of cases reported recently by several writers, one of whom estimates the



number as low as twenty-six. My observations are outlined in sequence in the accompanying chart. It will be noted that during the period from 1904 to 1927 thirty-one cases were reported, whereas from the year 1927 to June, 1929, fifty-eight cases were reported. This difference in the number of cases in the two periods suggests the possibility that no report was made on many of the earlier cases. Furthermore, the series of cases presented in later years by some operators are relatively large in contrast to those reported earlier, Mayer<sup>10</sup> citing nine cases in 1927, Bristow<sup>11</sup> eleven in 1928, Ollerenshaw<sup>12</sup> eighteen, and Campbell and Mitchell<sup>13</sup> ten in 1929. Some writers have mentioned that while some of their colleagues met with the lesion in their practice, they made no report of it.

Our experience with these cysts has been limited to two cases, which I add to the reported observations, bringing the total number of cases up to ninety-one.

To this list there should probably be added one case of a lesion of the external meniscus with cystic formation referred to by Bristow,<sup>34</sup> a second

*Table of Reported Cases of Cysts of the Semilunar Cartilages*

|  |      | External | Internal | Total No.<br>of cases |
|--|------|----------|----------|-----------------------|
| Ebner <sup>9</sup> . . . . .                         | 1904 | 1        |          | 1                     |
| Schmidt <sup>14</sup> . . . . .                      | 1906 | 1        |          | 1                     |
| Kroiss <sup>15</sup> . . . . .                       | 1910 | 1        |          | 1                     |
| Allingham <sup>16</sup> . . . . .                    | 1910 |          | 1        | 1                     |
| Eden <sup>17</sup> . . . . .                         | 1911 | 1        |          | 1                     |
| Riedel <sup>18</sup> . . . . .                       | 1915 | 6        |          | 6                     |
| Hammer <sup>19</sup> . . . . .                       | 1920 | 1        |          | 1                     |
| Ollerenshaw <sup>20</sup> (2 cases by Furniwall) . . | 1921 | 5        |          | 5                     |
| Phemister <sup>21</sup> . . . . .                    | 1923 | 2        |          | 2                     |
| Campbell <sup>22</sup> . . . . .                     | 1924 | 1        |          | 1                     |
| Jean <sup>23</sup> . . . . .                         | 1924 | 3        |          | 3                     |
| Fisher <sup>1</sup> . . . . .                        | 1924 |          | 1        | 1                     |
| Pelizaesus <sup>24</sup> . . . . .                   | 1926 | 2        | 1        | 3                     |
| Allison and O'Connor <sup>25</sup> . . . . .         | 1926 | 2        | 1        | 3                     |
| Tavernier <sup>26</sup> . . . . .                    | 1926 | 1        |          | 1                     |
| Zadek and Jaffe <sup>27</sup> . . . . .              | 1927 |          | 1        | 1                     |
| Edington <sup>28</sup> . . . . .                     | 1927 | 1        |          | 1                     |
| Mayer <sup>10</sup> . . . . .                        | 1927 | 6        | 3        | 9                     |
| Kleinberg <sup>29</sup> . . . . .                    | 1927 | 1        |          | 1                     |
| Heusser <sup>30</sup> . . . . .                      | 1928 | 3        |          | 3                     |
| Bristow <sup>11</sup> . . . . .                      | 1928 | 9        | 2        | 11                    |
| Pandalai <sup>31</sup> . . . . .                     | 1928 |          | 1        | 1                     |
| Ollerenshaw <sup>12</sup> . . . . .                  | 1929 | 14       | 4        | 18                    |
| Delchef <sup>32</sup> . . . . .                      | 1929 | 2        |          | 2                     |
| Campbell and Mitchell <sup>13</sup> . . . . .        | 1929 | 10       |          | 10                    |
| Nutter and Blew <sup>33</sup> . . . . .              | 1929 | 1        |          | 1                     |
| MacAusland . . . . .                                 | 1929 | 1        | 1        | 2                     |
|  |      | 75       | 16       | 91                    |

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case mentioned by Surls and Osgood,<sup>6</sup> and a third case of a polycystic fibroma of the external semilunar cartilage reported by Serafini,<sup>35</sup> of which I was unable to obtain a record.

*Personal Case of Cysts of Semilunar Cartilages.*—CASE II.—J. P., a man aged thirty years, had complained of pain in the region of the left knee for ten years. There was no record of injury. The man simply had noticed the presence of a small mass on the outer side of the knee at the level of the joint.

Examination was essentially negative except for a small semi-bony mass in the region of the outer cartilage. There was slight tenderness to deep pressure. The diagnosis of a cyst of the semilunar cartilage was given. The cyst and the cartilage were removed. Unfortunately a microscopical report could not be obtained owing to the over-decalcifying of the specimen. Four years after the operation, the patient had a perfect functional knee.

CASE III.—J. S., a man aged twenty-seven years, had complained of pain and stiffness in the left knee for two years, which had followed a fall while running. There was no swelling nor increase of fluid in the knee-joint. Motions were normal. In line with the joint there was a mass about the size of a small nut. There was no tenderness over the cartilage. A röntgenogram showed increased density in the line of the outer joint space. A cyst of the external semilunar cartilage was made as the diagnosis. The cartilage and cyst were removed. Three years after operation the patient had a perfect functional knee.

*Occurrence.*—Cysts occur far more frequently in connection with the external semilunar cartilage than the internal. In seventy-five of the ninety-one cases reported, the outer meniscus was the seat of the lesion. It is impossible to explain this predisposition of the external cartilage.

The age incidence varies from five or six years to the middle thirties, with the average age being between twenty and twenty-five years. Males are predominantly affected, in the relative proportion of three males to one female.

*Pathological and Histological Considerations.*—The cyst is approximately hemispherical in shape. In volume it may vary from the size of a pea to that of a good-sized prune. It is always of the sessile type, extending from one-half to one inch along the cartilage. The location of the cyst is fixed on the external border of the inner or outer cartilage, at about the junction of the anterior and middle thirds.

The cyst is multilocular and filled with a transparent gelatinous substance. Bristow<sup>11</sup> in his consideration of the pathology states that usually the swelling extends through the extra-synovial tissue and may also penetrate into the substance of the fibrocartilage itself. It is the opinion of some operators that the cysts are closely adherent to the capsule; Bristow, on the other hand, found that while the cysts penetrated deeply into the joint, they were not connected with the capsule. Rather, says Bristow, they "come forward from the synovial membrane and occupy the space usually filled with the extra-synovial fatty and areolar tissue.\*"

*Symptoms and Diagnosis.*—The patient complains of a dull ache in the knee and of some lameness. The pain is aggravated on movement, especially

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\* Bristow: Jones Birthday Volume, p. 273, 1928.

on acute flexion and complete extension. At times there is limitation of motion. In the region of the cartilage there is a visible swelling, which is firm and resistant to pressure and which may be tender. The cyst varies in size. It usually attains its maximum volume within a few weeks of its appearance, and then remains stationary. The cyst follows the cartilage in movement, and it is more prominent in extension than in flexion when it is drawn into the joint. These symptoms may be of a few weeks' or several years' duration.

The majority of writers are of the opinion that a cyst has never disappeared spontaneously. Campbell and Mitchell<sup>13</sup> question this view, since in one of their cases the tumor subsided after a short time, although the symptoms persisted; in another case the symptoms were recurrent; and in still another the tumor disappeared and the pain was relieved by aspiration of the contents of the cyst.

The clinical picture naturally suggests the internal derangements of the knee that are met with more frequently in practice. A careful examination of the swelling will establish the diagnosis. Usually the röntgenogram is negative, but it may show a shadow in the soft tissues in the involved region, as was seen in one of our cases.

*Treatment.*—The best treatment consists of the removal of not only the cyst itself, but also the affected semilunar cartilage, according to the regular technic used in removing an injured meniscus. Recurrences have been reported when the cyst alone was removed. Care must be taken in removing the cyst to preserve the joint capsule, for otherwise there will be difficulty in securing proper approximation. The after-care is similar to that following the usual operation for the removal of the meniscus.

The prognosis as to the complete recovery of function and strength in the knee depends, as in other derangements, upon the presence or absence of the structural changes within the joint. If the cyst has been of long standing, the pressure from it may have damaged the joint structures. In older individuals mild arthritic changes are usually present in the knee. The prognosis in these cases must, of necessity, be guarded. The outlook in cases of young patients is excellent, and in older patients is more favorable the earlier operation is performed.

*Symptoms of Cartilage Pathology.*—At the time of injury the patient always experiences severe pain. In addition, there is often a sensation of something giving way in the joint, and a definite click may be audible. In early teaching, locking was considered to be the most important diagnostic sign of cartilage pathology, but it is now clear that this clinical manifestation occurs with much less frequency. In our series locking was present in less than one-third of the cases. It is always present when fracture-displacement occurs. There is considerable effusion whether locking is present or not. Local tenderness is always present. In general, the symptoms resemble those of a sprain.

Following the initial trauma, the symptoms persist for several weeks.

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The acute pain passes away soon after the injury, leaving the joint aching and sore. Frequently there is pain in the region of the hamstrings and at the top of the patella, but the presence of this pain in no way indicates the extent of the damage to the cartilage. If the effusion is very marked, pain is present, but usually the effusion subsides in the course of two weeks.

The initial attack may be followed by others, some slight, some grave in character. While the recurrent attacks tend to be less severe than the primary one, conversely, they occur from only slight twists of the knee. Definite symptoms of pain, effusion, tenderness, and weakness accompany each attack. The effusion in repeated attacks is less and may persist for only a few days, but this intermittent effusion permanently damages the capsule and weakens the joint. If locking takes place in the subsequent attacks, it is usually transitory, and the patient soon learns to straighten the knee by manipulation. An individual experiencing recurrent attacks suffers intensely from the sense of fear that "something will give way in the knee," and, if the patient is young, he is deprived of the pleasure of participating in sports.

*Diagnosis.*—In the majority of cases, diagnosis of a derangement of the cartilage is not difficult, although it is practically impossible to make a definite decision as to the actual extent or location of the damage. A knowledge of the mode of production of a derangement is important. A detailed history of the case must be obtained, which in most instances will show a sudden onset of symptoms following an injury. Among the reliable diagnostic signs are slipping, local pain and tenderness over the site of the involved cartilage, effusion, swelling, locking of the joint, and the absence of the cartilage-thrust. Recurrent periods of disability with frequent slipping, a "sense of weakness or insecurity," and "fear that the knee will give way" are extremely important features. Usually the repeated attacks are less severe than the initial; on the other hand, they occur from slight injury.

The tenderness is marked in recent cases and may persist for months after the acute attack. It can be elicited by pressure on the articular line halfway between the internal lateral ligament and the patellar ligament, and in the region of the anterior end of the cartilage. Some tenderness may also exist slightly behind the centre of the internal margin of the meniscus. The determination of the presence or absence of the cartilage-thrust, which in the normal knee can be felt upon extension, is important in making the diagnosis. There is no difficulty in deciding upon this factor unless there are chronic thickening and tenderness throughout the inner capsule.

In long-standing cases, there may be some fluid in the joint, and one may elicit a slight click. Motions are usually normal, but if the joint is acute there is limitation of flexion, and forced extension is painful. If the cartilage is locked between the condylar surfaces, the knee cannot be straightened or fully flexed. If the injury has been extensive there is thickening at the attachments of the cartilage to the ligaments, and hypermobility is present. A chronic synovitis is present in a cartilage displacement.

While it has been stated above that it is almost impossible to arrive at a decision as to the exact pathology, in a certain proportion of cases one is able to determine definite mechanical changes sufficient to account for the symptoms and to warrant operative interference. For instance, in cases of hypermobile cartilages, there are usually irritative changes about the inner head of the tibia, due to the mild hypertrophy resulting from an injury in this region, or produced by the repeated passing of the loose cartilage over the tibial head. In cases of fracture of the meniscus there is a persistent sense of fear, an unwillingness to enter into sports, caution in going up and down stairs, and a certain weakness persists as in fractures of the carpal scaphoid. In displacements of the posterior cornu, there is usually no tenderness in the anterior aspect and there is more pain posteriorly.

Occasionally it is difficult to arrive at an exact diagnosis because of the presence of confusing symptoms, or because of the extent of the injury. In some cases the history may show an injury followed by periodic swelling, but there is no "giving way" of the joint and no pain. In other cases there may be little effusion following a severe injury, yet upon exploration the cartilage will be found torn. There is also a certain group of cases in which there is no history of a trauma or an infectious process, yet all the local symptoms of a cartilage derangement are present. In still other cases symptoms may point to an injury of the internal meniscus, but upon exploration the external cartilage is found to be involved.

Röntgen films in the anteroposterior and lateral planes and stereoscopic views of both knees should always be taken. While it is questionable whether röntgen films are of definite value in revealing actual cartilage pathology, they do rule out the presence of other lesions, such as calcified loose bodies, fractures, exostoses, or chronic arthritic changes. Dr. Arial George<sup>40</sup> concludes from an extensive study of the value of röntgen films in the diagnosis of cartilage derangements that, with special technic, it is possible to demonstrate the displaced meniscus in a majority of cases. He bases his opinion upon the fact that, in the average case, it is possible to visualize the normal internal or external cartilage or the shadow produced by it. He has made many dissections of amputated knees and found that the shadow he identified was the semilunar. Further he secured absolute proof by painting the semilunar specimen with white lead and taking further röntgen films. If this shadow is absent, the cartilage must be displaced. The greatest difficulty in demonstrating a displaced cartilage is that in many cases the cartilage has returned to normal position at the time of the röntgen examination. Therefore, it is only when the cartilage is still displaced that it can be demonstrated.

From my experience I cannot agree that cartilage pathology can be demonstrated as frequently as Doctor George states. In our cases röntgen films have seemed to be of value only when calcification had taken place.

Pneumarthrosis for the purpose of radiographic study is being used more frequently as a diagnostic aid, and some operators are finding it of value. Its

use should be limited to those cases in which a definite diagnosis cannot be made easily. Bircher<sup>41</sup> inflated nine joints with oxygen, carbon dioxide, or nitrogen gas, and secured positive findings of an internal semilunar injury in eight cases. Kleinberg<sup>42, 43</sup> believes that pneumarthrosis is a safe and simple test, but he reserves it for the study of doubtful lesions. He also stresses the importance of correlating the radiographic findings with the clinical examination.

*Differential Diagnosis.—Loose Bodies.*—Loose bodies can usually be felt as round masses by the patient, and they often move about in the joint. The symptoms, therefore, are seldom localized at one spot for any length of time. Pain and swelling are not acute unless the bodies cause locking of the joint. Locking, when it does occur, causes a sharper pain and more extensive swelling than in a semilunar derangement. The locking is only transitory, however, and is not caused by any particular movement of the joint. No tenderness exists over any particular area as in derangements. Röntgen films demonstrate a loose body that is calcified. The presence of more than one body helps to confirm the diagnosis.

*Lipomata* may give rise to locking of the joint, but the other symptoms accompanying this lesion do not resemble those of a cartilage derangement. Lipomata are usually associated with over-exercise rather than with trauma. When acute, they are tender and can be definitely outlined, usually on the outer side of the upper quadriceps pouch. The symptoms are mild and no pain is elicited on pressure.

*Osteomata* occur in hypertrophic joints. The pinching of the capsule and the locking of the joint may cause some confusion. A differential diagnosis is clearly made from röntgen films.

*Crucial Ligament Injuries.*—Rupture of the crucial ligaments usually occurs in severe injuries of the knee and is followed by rapid hæmorrhage and effusion. Not infrequently this tearing is associated with injuries of the internal meniscus and the internal lateral ligament. In severe injuries the actual pathology in the crucials may not be recognized until the joint is opened. In mild cases the presence of undue anteroposterior motion and lateral mobility with the knee in flexion suggests a crucial injury. If the anterior crucial ligament is ruptured, the lower leg can be displaced anteriorly, hyperextended, and rotated inward. When the posterior ligament is damaged, a less frequent injury, the tibia can be moved backward abnormally with the knee fully extended.

*Lesions of the Internal Lateral Ligament.*—Occasionally it is necessary to differentiate an isolated rupture or sprain of the internal lateral ligament from a deranged cartilage. As a rule, the ligament, which is very tough, is seldom damaged except in a severe injury which doubtless affects the meniscus at the same time. When differentiation is necessary, the location of the pain in the inner side of the joint and the tenderness over the attachments, particularly the lower attachment, as well as the free lateral move-

ment of the leg when the thigh is fully extended, are significant signs. There is no locking or other sign indicative of a meniscus damage.

*Bone Injuries.*—The diagnosis of bone injuries, such as fracture of the tibial spine, can usually be determined by röntgen films.

*Traumatic Bursitis.*—In traumatic prepatellar bursitis resulting from injury there is localized circumscribed swelling and fluctuation over the patella. Differentiation from an intra-joint lesion is not difficult.

*Hypertrophy of the Infrapatellar Fat Pad.*—Enlargement of this pad, so-called lipoma arborescens, is present in practically all knee-joint pathology, whether of traumatic or infectious origin. The pad can be observed and felt to be enlarged. Complete extension may cause pain. Following any exercise there is usually slight pain and effusion.

*Exostoses.*—Exostoses are common in arthritic lesions, occurring especially between the tibia and the femur on the inner side. They may give rise to painful pinching in the joint, but it is usually transitory and is not followed by effusion. Exostoses can often be felt clinically and can be definitely determined by radiographic examination. In most cases there are arthritic changes in other joints.

*Slipping Patella.*—It is often difficult in young girls to differentiate between a slipping patella and a derangement of the meniscus. The history showing the nature of the injury is important. Examination shows that with the leg at rest in flexion, the patella is found to the outer side of the knee-joint, but when the patient tires to get up or extend the leg completely, the patella suddenly snaps into place. An attempt to displace the patella is usually accompanied by a great deal of pain and fear.

*Synovial Membrane Lesions.*—The symptoms due to *synovial fringes*, while occasionally suggestive of a deranged cartilage, are not so acute at the initial injury, and they tend to be more localized. Creaking of the joint is common, and usually there is enlargement of the infrapatellar pad. Slight effusion follows each pinching. There is often a perceptible enlargement over the site of the local symptoms.

*A localized fold of synovial membrane* may be confused with a deranged semilunar cartilage. It is usually the result of synovitis and is a palpable membranous ridge.

*Traumatic Periosteitis of the Femoral Condyles.*—These cases, occurring as the result of a direct trauma, may be differentiated from a lesion of the meniscus by the location of tenderness on the condyle. In some cases there may be a flexion contracture.

*Prognosis.*—Three factors influence the prognosis: the number and severity of the attacks, the presence of arthritic changes, and the age of the patient. The average case, if treated properly following the initial injury, either by conservative or by operative measures as the case requires, obtains a resulting joint that is stable and painless without any restriction of movement. This is true of the adolescent case, the adult, or the young child. If

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a slight weakness or tendency to slipping persists in these cases that are treated early, it is probably secondary to a weak quadriceps.

In a long-standing case, the prognosis following operative removal of the cartilage must be somewhat guarded. The outcome from operation must of necessity be questionable in long-standing cases in which the meniscus is badly torn or comminuted. If the ligaments are relaxed as the result of repeated effusions, operation may restore motion to the joint, but instability persists. In any long-standing derangement, and particularly in those with numerous and severe attacks, arthritic or periarthritic changes take place, regardless of the age of the patient. It is impossible to predict an excellent result in such cases, for the removal of the cartilage will not overcome the arthritic changes. However, many of these neglected cases will be improved by the removal of the mechanical defect, and some functional improvement may be expected.

In elderly cases in which the cartilage changes are often secondary to a local arthritis, the prognosis is poor. Usually these patients are under-nourished, and the arthritic process involves several joints. Some type of protective apparatus is the best form of treatment.

In our series of cases, in some of which operation was performed following the primary injury and in others following repeated attacks, satisfactory results were obtained in about 91 per cent. Motion and functional use were regained. In the few instances in which there was a recurrence of symptoms, the cause could not be attributed to the cartilage pathology, but rather to the presence of some other lesion, such as a loose body, which was overlooked at operation.

Cases in which a definite diagnosis is made and operation advised, but refused by the patient, often develop severe hypertrophic changes in later life. In view of this danger, the importance of early operation is to be appreciated.

*Treatment.*—The nature of the treatment depends in the average case upon whether the attack is the initial or a recurrent one. The primary attack, if slight and accompanied by no mechanical changes, can often be treated satisfactorily by conservative measures. Severe initial injuries, or recurrent cases presenting a definite history of injury and typical symptoms of an acute nature, call for operative interference.

*Conservative Treatment.*—Subsequent to an injury, the knee, if not locked, should be immobilized in extension to prevent all movement. If necessary, fluid can be aspirated. The duration of the period of immobilization varies according to the severity of the injury. In the average case it is three weeks. This procedure is imperative regardless of how slight the injury or how mild the symptoms. Very often a blow or twist will cause only slight disability and there may not even be fluid in the joint. Unfortunately, the treatment of these slight injuries is frequently disregarded.

When locking has occurred, reduction of the displaced cartilage followed by immobilization is the routine procedure. The displacement is easily



recognized by the flexed position of the knee and the presence of pain in the region of the cartilage on any attempt at forced extension. Reduction should be made as early as possible before repair tissue has organized and before the cartilage has undergone changes in shape from pressure.

The method of reduction is not important provided extension is obtained. It is most essential, however, for the surgeon to make sure that complete extension has been obtained. Upon the accomplishment of reduction, the pain disappears, the knee can be held voluntarily in complete extension, and the patient is confident that the correction has been made. In the majority of cases reduction is simple, but in long-standing cases it may present difficulty, and occasionally it may be necessary to repeat the process several times, even under an anæsthetic.

The method of reduction used in our clinic is the Jones<sup>44</sup> procedure, consisting of movements of acute flexion and lateral deviation and rotation inward to open the joint space, followed by full extension. A firm flannel bandage is then applied from the mid-calf to the mid-thigh, with the knee straight. This is worn for protection as long as the fluid persists, usually for a period of a week or ten days. Baking, massage, and gentle passive motions are then begun. Walking is allowed in a week or ten days, depending upon the sensitiveness and swelling. Strain upon the internal lateral ligament and repair tissue is prevented for several months by wearing a lift on the inner side of the sole and heel, which forces the patient to walk with the foot inverted.

The majority of primary cases of the hypermobile type respond to this treatment. The fractured cartilage eventually comes to operative treatment. The recurrence of symptoms in some cases has been explained by Fisher<sup>1</sup> on a physiologic basis. He noted that the peripheral margins of the cartilage, where the blood-supply is greater, recover more quickly from an injury than the concave edges or the centre of the cartilage, which are not so well nourished. In fact, repair may fail to take place in the central and inner parts. Fisher also discovered that in fractures the edges of the fragments became smooth and rounded and even after a long period of immobilization they did not unite.

*Operative Treatment.—Indications.*—Following an initial attack that has left the joint locked in flexion, which cannot be reduced by manipulation, removal of the cartilage by operation is necessary.

Operation is the only means of cure in recurrent cases presenting a definite history of injury followed, upon slight provocation, by an intermittent return of the symptoms of pain, slipping, and tenderness. A chronic or recurrent synovitis is indicative of a pathological change within the joint. Failure to remove the cartilage in these cases not only leaves the patient physically handicapped, but there is the probability that the presence of this derangement will lead to joint changes. (See section on "Prognosis.")

In the presence of arthritic complications, the advisability of operation must be considered carefully, for arthrotomy is not warranted if the patient

will not receive benefit. Several influencing factors are the age of the patient, the location of the arthritic lesion, that is, whether monoarticular or generalized, the stage of the infection, and the part played by the cartilage derangement and the arthritic element in producing the present symptoms. If the changes are localized and the disease is progressing, removal of the source of irritation is imperative.

In a certain proportion of cases in which it is impossible to determine pathology sufficient to cause the existing symptoms, the advisability of exploratory arthrotomy must be considered. One must weigh carefully the symptom complex and the physical manifestations, and one must appreciate the seriousness of irritative changes of mechanical origin.

*Technic.—Pre-operative Care.*—In view of the atrophy of the quadriceps, which is present in the average case, it is well to carry out a course of muscle-training for this group before operation. The patient, by contracting the quadriceps voluntarily fifty times, several times daily, both before operation and early in the convalescence, even before passive motion is started, can aid in hypertrophying this muscle. Not infrequently the persistence of weakness after operation is due to the loss of musculature, a weakness that the patient cannot differentiate from the original cartilage symptoms.

The preparation for arthrotomy of the knee must be carried out meticulously. While knee-joint surgery, through the introduction of careful asepsis and the development of perfect operative technic, has progressed to the stage where it is no longer avoided, still every precaution must be taken, as the knee does not tolerate infection.

The patient enters the hospital two days before operation. The leg from the ankle to the groin is given a dry shave, washed with soap and water for ten minutes, and scrubbed with alcohol and ether. On the night before the operation, the leg from the ankle to the groin is painted with 3 per cent. iodine, the leg is held elevated until dry, and a sterile dressing is then applied, which remains on until the patient is on the operating table. A final preparation of 5 per cent. iodine is given to the same area just before operation.

*Excision of the Cartilage.*—Rigid asepsis must be practised. A tourniquet is applied to prevent operative hæmorrhage. During the application of the tourniquet, the surgeon is careful not to touch the skin. The knee is properly draped, and flexed over the table at an angle of 90 degrees. A sterile towel is placed over the knee, through which the line of incision is determined and marked by thumb pressure (Fig. 9). The towel is then removed, and an incision made. Various types of incisions are in use, including the transverse, the vertical, and the curved. Most incisions tend to penetrate the joint between the patella and the corresponding lateral ligament. Some operators recommend a longitudinal patellar incision with division and displacement of the patella, and find that it gives satisfactory exposure. The particular type of incision is not important provided it allows sufficient exposure of the meniscus, makes possible its removal, and

permits inspection of the remainder of the joint. We advocate either the curved incision of Jones<sup>44</sup> (Fig. 10), or a modification of it. In view of the advisability of examining both cartilages, since not infrequently it is impossible to determine from the location of the symptoms which meniscus is affected, a modification of the Jones incision which permits direct vision to both cartilages has been adopted as the routine procedure in our clinic. This incision begins above the inner condyle, crosses the patellar tendon without severing it, and terminates on the external condyle at a point opposite the point of origin.

The knife is then discarded, and the skin swabbed first with a sponge



FIG. 9.—Excision of the semilunar cartilage. Determination of line of incision through towel.

that has been wet in Harrington's solution, and then with a sponge that has been wet in salt solution. Towels are now clamped over the skin to prevent touching it during the remainder of the operation.

With a fresh knife, an incision of sufficient length to allow proper exposure of the cartilages is made through the fascia, synovial membrane, and joint capsule, in the same line as the original incision. Care is taken not to cut the patellar tendon. Pathological changes in the capsule as well as the amount of fluid are noted. The joint is exposed, and a thorough inspection made of the interior. I want to place particular emphasis upon the

examination of the joint region. In addition to the derangement of the cartilage, there may be contributing pathological factors, such as loose bodies or enlargement of the fat pad, which are likely to be overlooked if the exploration is not complete. The persistence of any pathology in the joint may lead to a recurrence of the symptoms. In my opinion, the joint cavity should be explored with the gloved finger, for only by this method is it possible to determine the presence of loose bodies. (This step is not approved by some of my colleagues, but I believe that if the technic is carried out carefully there is no danger in the procedure.) To complete the inspection, the other cartilage and the crucial ligaments are examined.

The cartilage is now dissected from its attachments (Fig. 11). Regardless of the extent of the pathology in the cartilage, total excision is generally advisable. Even when the cartilage is found to be hypermobile, it is well to remove the entire meniscus. Rarely in a fracture of the anterior tip of the cartilage, when the posterior part remains firmly attached, removal of the broken tip alone is justified.

During the removal of the cartilage it is kept under tension. To obtain better exposure it is often advisable to rotate the tibia inward or outward, or to pry the femur from the tibia with a blunt dissector. The anterior end of the meniscus is loosened by means of a sharp knife and removed. The ends are grasped with heavy Ochsner snaps and held tightly. The dissection now follows along the internal lateral ligament. The posterior part is cut with scissors whose curve conforms to the convexity of the table of the tibia. Care must be taken not to injure the femoral cartilage, the lateral ligament, or the crucials.

The joint is then examined for fat tabs, loose bodies, lipoma, or other pathology. In chronic knee-joint lesions the infrapatellar fat pad is often enlarged, and the removal of the entire structure or a large part of it is advisable. Hypertrophic bony changes are rarely interfered with, for once the irritating factor has been removed, spurs tend to be absorbed or their sharp edges become rounded, thereby lessening the irritation.

Throughout the operation sponges are used only once. It is not necessary to wash out the joint as no hæmorrhage will occur if a properly applied Esmarch bandage has been used.

The wound is closed in layers; the synovial membrane is sutured with interrupted fine catgut, the capsule with interrupted catgut No. 2, the fascia with continuous catgut No. 1, and the skin with silkworm gut or catgut. A sterile dressing is applied from the mid-calf to the mid-thigh.

The tourniquet is not removed until the flannel bandage has been applied to produce slight compression. By this means any oozing into the joint following the removal of the tourniquet is avoided. Unquestionably hæmorrhage into the joint is responsible for much of the post-operative stiffness occasionally seen.

The same technic is used for the removal of the external cartilage.



FIG. 11.—Excision of the semilunar cartilage, showing the exposure of the cartilage. The skin edges are clamped off, and the cartilage is being excised with a tenotome.



FIG. 10.—Excision of semilunar cartilage, showing depressions made by knife handle, the line of incision and the bony landmarks dotted.

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*After-treatment.*—In past years, it has been our custom to secure immobilization by means of a plaster bandage, which was worn for a period of two weeks. Complete immobilization has a certain advantage as far as the patient is concerned in that the pain is lessened. Of late, we are inclined to believe that this period of immobilization in a plaster bandage predisposes the formation of adhesions. To avoid this complication, we are applying a snugly fitted voluminous flannel bandage from the toes to the hip with considerable reinforcement about the knee-joint. This bandage holds the knee snugly, and by producing compression prevents any extravasation of fluid and hæmorrhage subsequent to the operation. In addition, the bandage, as it begins to loosen, allows a little freedom of motion during the first week after the operation. Our experience with this procedure thus far seems to bear out our view that it is preferable to complete post-operative immobilization.

The duration of the convalescence depends entirely upon the pathology. Recovery from a hypermobile or torn cartilage that has been treated promptly takes place within a few weeks. Arthritic cases, on the other hand, recover more slowly. In the simple case the compression bandage is worn for ten days or two weeks. As soon as the temperature is normal and the patient is comfortable, he may begin to walk with crutches. At the end of two weeks, hot fomentations and gentle active movements are carried out daily, and speed up the convalescence. In three weeks the patient should be able to bend his knee to a right angle. Massage of the thigh and calf should be instituted as early as possible. In eight weeks most patients are able to resume moderate activity. Other patients recover much sooner. I have known a juggler to return to the circus at the end of three weeks. Convalescence is likely to be slow in industrial cases, as these patients may be influenced by the fact that they are drawing compensation as long as they are disabled, and they are, therefore, loath to use their muscles from fear of pain.

Correction of a talipes valgus or a weak foot should be practised as a routine procedure, following the removal of the cartilage, in order to prevent strain on the internal lateral ligament. A lift on the inner side of the heel and sole may be used for this purpose.

### AN ANALYSIS OF 388 OPERATIVE CASES

This series of 388 cases extends over a period of twenty-five years; the most recent case is dated December 31, 1929. Seven associates performed the operations.

A searching questionnaire was sent to all patients upon whom operations had been performed before July 1, 1929. No attempt was made to ascertain the post-operative results in cases in which at least five months had not elapsed since the operation. Direct replies, or information from reliable sources, were received in 287 cases. These data have, in each case, been correlated with the pre-operative findings available, as well as with the

pathology disclosed at operation. As it has not been possible to obtain a complete history of each case, our report on the different findings must, of necessity, be based upon varying statistics. A statement as to the exact number of cases recorded will, therefore, be found in each section.

*Sex, Age, and Joint Involvement.*—Two hundred and fifty-two cases, or 65 per cent. of the series, were males.

The age distribution, as determined from the 349 case records available, showed the average age at the time of operation to be twenty-one years. Thirty-two per cent. of the patients were between the ages of twenty-one and thirty; 23 per cent. were between eleven and twenty years; and 17 per cent. were between thirty-one and forty years of age. There were two cases younger than ten years, and there were eight cases between the ages of sixty-one and seventy.

The right and left knee were involved almost equally; in fact, in the series of 363 records obtainable, there were 181 involvements of the right knee and 182 of the left knee.

*Etiology.*—The etiology was found recorded in 355 of the 388 cases. In 87 per cent. trauma was the specific etiological factor. By far the majority of the injuries were of an indirect nature, including wrenches, twists, and sprains. Falls held a prominent place in the etiology. Many of the derangements were sustained during activity in sports, particularly in football and basketball. In five cases the disturbance was due to disease, tuberculosis of the knee-joint being the underlying cause in one case, and hypertrophic arthritis in four cases. In thirty-nine cases the cause was unknown; there was apparently no history of injury and no manifestation of disease. The presence of a lesion within the joint was indicated by the symptoms of pain, either of acute or slow onset, swelling, and local tenderness.

*Symptoms.*—The incompleteness of the pre-operative records and the fact that, during the period of twenty-five years over which this series extends, emphasis was placed on different symptoms at various times, make it impossible to compute exact statistics on the manifestations of the derangements. From approximate calculations, the most characteristic symptoms were pain, weakness, and tenderness over the site of the affected cartilage. Locking occurred in nearly one-third of the cases, and it was present in several cases at the time of operation. Many patients complained of a "sense of derangement," a "giving way," or "something slipping in the knee," and in a few cases there was an audible click. Swelling was noted in about one-fourth of the cases. Limitation of motion, lameness, and stiffness were mentioned in only a small percentage of the cases. Practically all patients had experienced recurrent attacks of disability.

The duration of the symptoms varied from a few days in six cases to more than thirty years in one case. The number of patients who had had trouble for a period of years amounted to 163, and the majority of these had suffered between one and four years. One hundred and thirty-four

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patients had had symptoms for a period varying from one to twenty months, and thirty-nine patients had been disabled from one to ten weeks.

*Pathology.*—The internal cartilage was involved in 276 cases, the external in thirty-eight cases, and both cartilages in the same joint in forty-seven cases. No record was made in twenty-seven cases.

The pathological findings were checked in 435 instances, which included the forty-seven cases in which both cartilages were involved. Records were found in 362 cases, but unfortunately they are brief in many instances. One hundred and forty-six cartilages, or 34 per cent. of the series, were listed as hypermobile. This percentage might have been lower if complete notes had been made, stating whether a marginal or posterior fracture existed. One hundred and forty-nine cartilages were fractured, but the site of the tear was not always designated. Nineteen were located at the anterior tip, thirteen in the anterior half, seven in the middle, and ten in the posterior half. Three cartilages were split from the anterior to the posterior end. While the bucket-handle type of fracture is mentioned in only five cases, it undoubtedly existed in many more, probably in as many as fifty cases. There were fifty cases of displaced cartilages. Five cartilages were totally avulsed. In addition, the menisci were swollen and thickened, and a few were calcified. Some cartilages were so altered that they could hardly be identified. Loose bodies, fat tabs and lipomata were excised in several cases. Hypertrophic changes were noted in several cases, findings that usually explained an unsatisfactory result. Capsular thickening was noted in some cases of long standing.

*End-results.*—The results have been considered from the following points of view: 1, satisfaction of the patient; 2, recurrence of the trouble; 3, limitation of movement; 4, stability; 5, comparative strength of the two knees; 6, pain and discomfort since the operation; 7, the period of convalescence; 8, traumatic or infectious involvement of any other joint since operation; and 9, occupation of the patient.

Three hundred and seventy-two questionnaires were sent out, and 287 replies were received. It was impossible to obtain information on the other cases. Inquiries were not sent to eight patients who had had operations too recently, nor to eight patients who, in view of the complications existing at the time of operation, could not possibly have obtained joints which they would consider satisfactory, although in some instances they might have secured relief from the cartilage symptoms for which the operation was performed. This latter group will be discussed farther on in the paper.

In 223 cases, one to ten years had elapsed since the operation, and in fifty-five cases, ten to twenty-five years had elapsed. In forty-one cases, there was an interval of five to ten months between the operation and the time of inquiry. Eight cases were not checked because the operation had been performed too recently. The time interval was unrecorded in sixty-one cases.

The duration of the average convalescent period was six months.



Of the 287 patients who replied to the questionnaire, 230 or 80 per cent. expressed satisfaction with the result. Twenty-eight patients stated that they were not entirely satisfied and twenty-nine were dissatisfied.

Ninety-six patients of the "satisfied" group reported that the result was perfect, and the knee normal in every way. One hundred and six patients in this group stated that they experienced slight symptoms from time to time; the leg pained slightly in inclement weather, or it tired easily or was numb, or the patient felt the need to favor it. Such symptoms were so slight as to be practically negligible. Four patients who had had the operation only five months previously complained of slight symptoms, but the prognosis in each case is excellent. There were twenty-four patients in this group who, while they expressed satisfaction with the result, complained of definite pain, instability in walking or running, limitation of motion, or weakness.

Interesting notes were made in the questionnaires by some of these patients of the "satisfied" group. Practically all of them had returned to their former occupations regardless of how strenuous they were. One patient climbs trees, carrying heavy loads; another schools ponies all day; several patients walk many miles a day without discomfort; and others are active in sports of all kinds.

The results in the cases in which definite symptoms were present, although the patient considered the outcome satisfactory, as well as the results in the questionable and unsatisfactory cases were carefully investigated. In the study of these cases it is necessary to consider whether the operation has been satisfactory not only from the point of view of the patient, but also from the surgeon's standpoint. Not infrequently, one is called upon to remove a cartilage presenting a predominance of symptoms in the presence of a coëxisting disease or other pathology. In such cases operative interference cannot offer entire relief to the patient, but the cartilage symptoms are checked, a more stable knee is obtained, and often the condition of the entire joint is benefited by the removal of an aggravating factor. It is most likely that the patient in judging the outcome of the operation is unable to discern between relief from the symptoms due to the cartilage derangement and those due to the existence of other pathology, with the result that unless normal function has been obtained, he condemns the operation. There are other cases in which the after-care was neglected, or a second injury complicated the result, or the patient was influenced in replying by the fact that he had a case under litigation.

In the series of 287 cases there were thirty-four cases complicated by the presence of arthritic symptoms; some cases showed mild or severe hypertrophic changes at the time of operation; others had a generalized arthritis, existing either before the operation or developing afterward, and while the infection was not located definitely within the joint it undoubtedly had a deleterious effect upon it; and in still other cases a monoarticular arthritic joint had existed. Sixteen of these patients considered the operation satisfactory, although they still experienced symptoms of an arthritic

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nature. Fifteen patients, four of whom were only partly satisfied with the result and eleven of whom expressed dissatisfaction, upon examination, showed that the cartilage symptoms had been relieved and the joints generally improved. From the surgeon's standpoint, therefore, arthrotomy had been warranted and the results might be considered satisfactory. In the three other cases the arthritic element was so severe that it was impossible to judge the result of the cartilage operation.

There were eleven cases in which, in addition to the cartilage derangement, other pathology was present. Among these lesions were damage or weakness of the ligaments or tendons, congenital dislocation of the patella, osteochondritis of the femoral condyle, decussation, and fracture of the tibia. This fracture case was a severe one of the tuberosity of the tibia which allowed a 45 degree knock-knee and had existed for six months to a year. In the presence of such diffuse and long-standing pathology the knee could not be restored to normal, but the result in so far as the removal of the cartilage symptoms was concerned was satisfactory. Four other cases showed upon examination that they had improved sufficiently and had such a favorable prognosis that they might be considered satisfactory by the surgeon. Six patients reported that they were satisfied with the outcome.

There was still another group of cases in which the results reported by the patient as "partly satisfactory" or "unsatisfactory" proved upon examination to be satisfactory from the surgeon's point of view. In one case muscle disuse accounted for the unfavorable reply; examination showed that the result was an unusually good one and the prognosis is excellent. One patient who had suffered a great deal since the operation with ulcers of the stomach and intestine could not consider the knee condition with an open mind; examination showed the knee to be satisfactory in every way. One boy sent a "partly satisfied" reply, but his mother wrote that the result is excellent. Another result was good considering that the patient was extremely active in his position as an instructor in soccer. Another result was satisfactory in view of the fact that the symptoms had been present for twenty years before the operation. In four cases replies of "partly satisfactory" were undoubtedly given for ulterior motives, as these patients were seeking compensation from insurance companies. There were two cases in which the operations had been performed only five months previously; they have an excellent prognosis, and the patients stated that if the improvement continues they will be satisfied with the result. One patient had an excellent result and there is no explanation for his reply.

The results in six cases, after investigation, can be considered only partly satisfactory. One patient had good function, but there was some circulatory disturbance. One patient had a quadriceps paralysis, which, however, was clearing up, and, in fact, at the time of this report two-thirds of the normal power has returned. In a third case there was quadriceps weakness following the operation. In three cases the results were clinically perfect, but symptomatically not quite normal.

There were fourteen poor results inclusive of a case that became septic. Nine patients had definite recurrence of the former trouble, indicating that other pathology, such as involvement of the other cartilage, a tab, or a fringe, was present. One cannot place too much emphasis on the importance of thorough inspection of the joint at the time of operation. Some of these cases are now under observation pending a decision for a second arthrotomy, which, had thorough examination of the joint been made at the first operation, could have been avoided. Two other patients in this group complained of constant pain, the presence of which could not be explained. One patient had an unstable knee, and another had limitation of motion, instability, and pain.

It is impossible to classify six results. In one case a blood-stream infection set up two weeks following the operation, and the knee became septic. The process cleared up, leaving the joint somewhat limited in motion. The prognosis is good. One patient left the hospital against advice; another went to an osteopath for after-care; another suffered a strain of the knee two months after the operation; one had had symptoms so long that a good result could not be expected; and one joint was tuberculous.

In regard to the eight cases in which questionnaires were not sent, one patient had developed a post-operative sepsis (the only case in the entire series), one case, in which a tuberculous process was suspected at the time of operation and confirmed later by a pathological examination, developed into a tuberculous joint, and one case subsequent to operation developed into a Charcot joint with its usual course of symptoms. The advisability of operation in a possible tuberculous or syphilitic case should be considered carefully, for sufficient benefit would not be secured to warrant the arthrotomy. In the two instances cited the operation was hardly justified. There were three cases of general arthritis. One other case was complicated by a severe fracture, and another patient had an intermittent hydrops and the removal of the cartilage was merely incidental in treatment.

*Summary.*—After this investigation of the results, in which all the factors that might influence the outcome of the operation were considered, one may conclude that the operative results were more satisfactory than is indicated by the statistics based upon the patients' replies. Two hundred and sixty-two results, or 91 per cent. of the series of 287 cases, were satisfactory from a scientific and clinical standpoint; six cases were partly satisfactory; thirteen cases could not be classified; and fourteen results (including eight cases in which no questionnaires were sent) were poor.

#### CONCLUSIONS

1. The removal of a semilunar cartilage according to the technic described is followed in the majority of cases by a result entirely satisfactory to the patient.

2. The best results are obtained in cases of young adults when the offending cartilage is removed within a short time of the trauma.

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## SUMMARY CHART OF CASES

| No. of cases | Sex            | Age               | Knee involved     | Cartilage involved | Etiology            | Pathology            | Time between onset and operation | Time since operation   | End-results                                |
|--------------|----------------|-------------------|-------------------|--------------------|---------------------|----------------------|----------------------------------|------------------------|--|
| 388          | Males<br>252   | 8-10 yrs.<br>2    | Right<br>181      | Internal<br>276    | Trauma<br>311       | Hypermobile<br>146   | Days<br>6 cases                  | 5-10 mos.<br>41 cases  | <i>From patient's viewpoint</i>            |
|              | Females<br>136 | 11-20 yrs.<br>81  | Left<br>182       | External<br>38     | Disease<br>5        | Fractured<br>149     | Weeks<br>39 cases                | 1-10 yrs.<br>223 cases | Satisfactory 230<br>Partly satisfactory 28 |
|              |                | 21-30 yrs.<br>112 |                   | Both<br>47         | Cause unknown<br>39 | Dislocated<br>50     | Months<br>133 cases              | 11-25 yrs.<br>55 cases | Unsatisfactory 29<br>Unrecorded 101        |
|              |                | 31-40 yrs.<br>62  |                   |                    |                     | Totally avulsed<br>5 | Years<br>164 cases               |                        | <i>From surgeon's viewpoint</i>            |
|              |                | 41-50 yrs.<br>49  |                   |                    |                     |                      |                                  |                        | Satisfactory 262<br>Partly satisfactory 6  |
|              |                | 51-60 yrs.<br>35  |                   |                    |                     |                      |                                  |                        | Unclassified 13<br>Poor 14                 |
|              |                | 60-70 yrs.<br>8   |                   |                    |                     |                      |                                  |                        | Unrecorded 93                              |
|              |                | Un-recorded<br>39 | Un-recorded<br>26 | Un-recorded<br>27  | Un-recorded<br>34   | Un-recorded<br>85    | Un-recorded<br>46                | Un-recorded<br>69      |  |
|              |                |                   |                   |                    |                     |                      |                                  |                        |  |
|              |                |                   |                   |                    |                     |                      |                                  |                        |  |
|              |                |                   |                   |                    |                     |                      |                                  |                        |  |

3. A guarded prognosis must be given in cases with any arthritic tendency, which include cases of long standing that show definite hypertrophic changes at operation, and cases of older patients, that is, those beyond middle life.

4. Particular attention should be given to the treatment of mild injuries. If a slightly damaged cartilage is neglected, it exposes the joint to progressive arthritic lesions.

5. The most reliable diagnostic features are: *a.* A definite history of trauma. *b.* Recurrent periods of disability with local pain, slipping, effusion, and swelling, initiated usually by some minor injury or twist. *c.* Acute local tenderness at the point of attachment of the cartilage where the damage is located, with a tendency for the tenderness to persist at this point. *d.* Locking, that is, the sudden inability to extend the joint fully. *e.* The absence of the cartilage-thrust.

6. The presence of an early pathological lesion such as tuberculosis or syphilis must be borne in mind when operation for the removal of the cartilage is advised.

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# BENIGN TUMORS OF THE TENDON SHEATHS OF UNUSUAL SIZE

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THE benign tumors of the tendon sheaths, which have gone under the name of xanthosarcoma, spindle-cell sarcoma, myeloid tumor, myeloid endothelioma, myeloxanthoma, granuloma, and giant-cell sarcoma, were first reported by Von Chassaignac in 1852.<sup>1</sup> Heurtaux,<sup>2</sup> in 1891, was the first one to differentiate these benign tendon-sheath tumors from the sarcomas, in that they follow a definite, benign course, whereas sarcomas are malignant in character. Heurtaux named these benign growths myelomas.

Although most of the authors agree to the fact that these tumors are benign growths, there is still a difference in opinion as to their histogenesis whether they are granulomas or true neoplasms.

Arzt,<sup>3</sup> Broders,<sup>4</sup> Ely,<sup>5</sup> Fleissig,<sup>6</sup> Janik,<sup>7</sup> and Ollernshaw<sup>8</sup> conclude that these tumors are granulomatous in nature, this conclusion being based upon the assumption that the giant cells present in the tumor masses are foreign body giant cells produced by the constant irritation of the tissues by the cholesterin deposits.

Bellamy<sup>9</sup> and Stewart and Flint<sup>10</sup> believe that the tumors are endothelial in origin and that too much stress has been laid upon the finding of cholesterin deposits, regarding them possible etiological factors for this tumor growth.

Targett,<sup>11</sup> in 1897, thought these tumors to be spindle-cell sarcomas but was unable to explain the presence of the giant cells. He emphasizes, however, that "the relation of these tumors to inflammatory processes need not be discussed, since they are neither tuberculous, syphilitic, or granulomatous clinically as well as histologically."

Dor,<sup>12</sup> in 1898, was first to describe the xanthomatous cells in the xanthosarcoma and this led him to believe that he was dealing with a mixed tumor composed of xanthomatous and myeloid tissue. He also believed that the presence of these two types of cells was brought about by a different histological development of a common cellular element.

Tourneaux,<sup>13</sup> in 1913, calls the tumors under discussion sarcomas of a low malignancy. Harbitz<sup>14</sup> and Buxton<sup>15</sup> regard them as benign, since they do not recur after thorough removal, nor do they form metastases. They also maintain that the tumors are mesothelial in origin.

Shattuck<sup>16</sup> discusses the possibility that giant-cell myelomas of the tendon sheaths are the same kind of myelomas that occur at the ends of the long bones. He explains them on the basis of persistent growth of bone elements displaced, during embryonic life, into the tendon sheaths which are continuous with the bone.

Albertini,<sup>17</sup> in his recent work upon this subject, in which he gives an exhaustive résumé of the literature, has demonstrated that in all giant-cell tumors the ground tissue exhibits the structure of mesenchyma, and the giant cells which characterize them are, like spindle cells, mesenchymal forms whose protoplasm has not undergone division. He believes that the abundant capillary network in all giant-cell tumors is formed from the mesenchymal reticulum of the ground tissue which has undergone a kind of canalization because of the blood entering it. Accordingly, if the abundance of vessels in the tumor tissue does not arise from budding, as in inflammation, the support for the

granulomatous nature of the tumor falls to the ground. He denies that the giant cells are wasted vascular germs, but that they are intertwined with the retiform tissue, and, owing to the canalization of the retiform tissue by the blood, they undergo transformation into cells resembling endothelium and thus come to lie in the opening of the blood spaces.

Since the anatomic and clinical characteristics speak against the sarcomatous nature of these tumors, Albertini, therefore, discards both the sarcoma and granuloma hypotheses and names these growths "benign xanthomatous giant-cell tumors of the tendon sheath."

The tumors are usually relatively small. Only in a few instances do they reach such an unusual size as in the cases to be reported. The first is interesting not only because of its large size but also because of its tendency to cause atrophy of bone by pressure and to invade the bone. Through a search of the literature on the subject, I read of six cases in which the bone was



FIG. 1.—X-ray showing the extent of bone atrophy and erosion due to pressure and invasion of the tumor mass

involved in this type of growth. One case, described by Venot,<sup>18</sup> showed the tumor springing by two pedicles from the palmar surface of the middle and terminal phalanx, respectively, and ending up in a large tumor mass in and around the tendon sheath. This condition led Venot to consider the tumor growth as a primary osseous growth. A second case was reported by Ely<sup>5</sup> in which he describes a xanthosarcoma existing in both bone and tendon sheath in the region over the lower end of the fibula.

#### REPORT OF CASES

CASE I.—Steve M., aged twenty-two, laborer, was admitted to the Cook County Hospital, Chicago, Illinois, August 22, 1929, with a complaint of swelling in the left foot for a period of three years. The patient stated that he was perfectly well until three years ago, when he noticed, without any apparent cause, a small nodular swelling on the lateral side of his left foot. The swelling has gradually increased in size but has never broken down nor discharged. The swelling has caused very little pain but much discomfort due to its size. The patient was a white adult male who was not acutely ill

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and presented as the essential finding a swelling in the left foot about the size of an orange. This tumor extended into the lateral three toes. The mass was immovable and had no signs of inflammation such as redness or heat. Popliteal or inguinal glands were not palpable.

The X-ray picture (Fig. 1) reveals the shaft of the metatarsal bone of the fourth toe completely destroyed or rather replaced by a new growth, and as it approaches the epiphyseal ends, bone fragments become visible. There is a marked atrophy of the first or proximal phalanx of the same toe. The third toe adjacent to the fourth toe shows pressure atrophy of the metatarsal bone and is also convexed medially. A lateral X-ray picture shows a dorsal convexity of the metatarsals due, possibly, to the force exerted by the tumor upward against the bone.

August 29, 1929, a longitudinal incision was made over the fourth metatarsal bone. The skin was reflected from the tumor mass and the mass was separated by dissection from the surrounding tissues. The fourth metatarsal bone was imbedded in the tumor

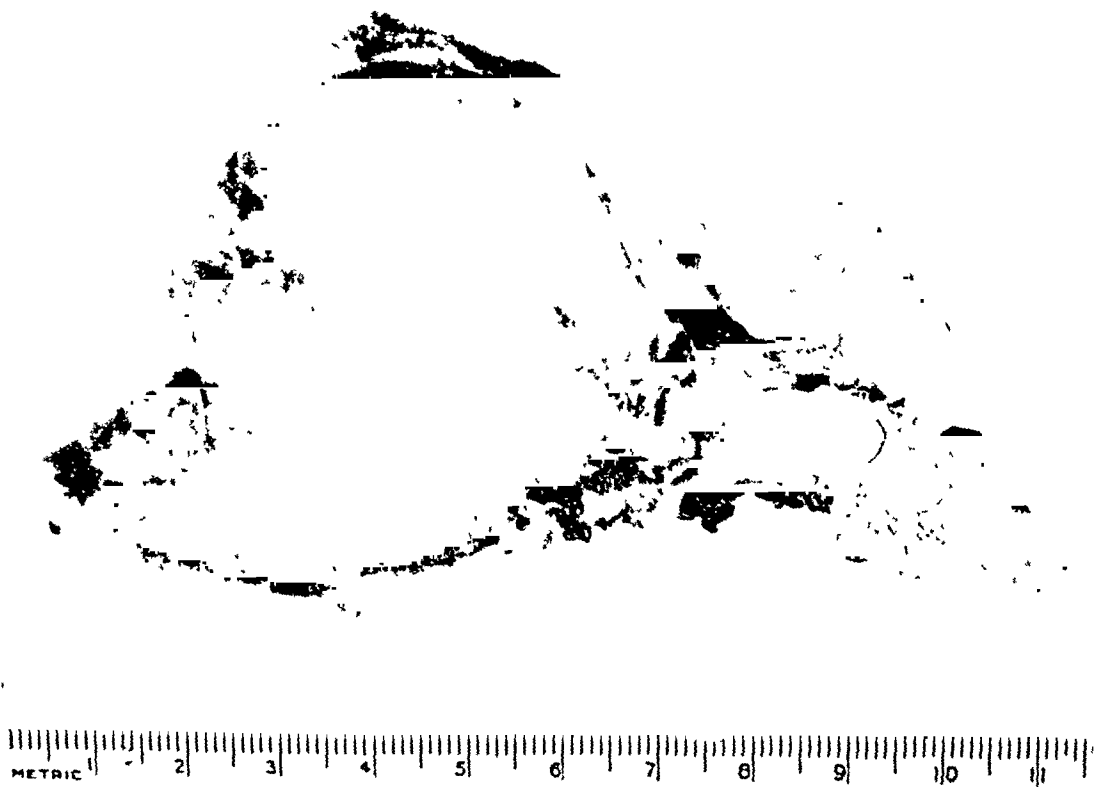


FIG. 2.—Case I. Showing extent of tumor mass with erosion and distortion of the metatarsal bone.

mass and was removed en bloc along with the fourth toe. The patient made an uneventful recovery and was discharged on September 4, 1929. He was last heard from May 28, 1930, and he states that he has not noticed any recurrences of growth.

*Gross pathological description of specimen.*—The specimen consists of a toe of the left foot amputated at the proximal portion of the metatarsal bone. The toe (Fig. 2) is completely replaced, except for the distal phalanx, by a grayish-white mass which is elastic and moderately firm. This mass completely envelops both the dorsum, lateral and plantar surfaces of the toe. The portion of the tumor that is bare of epidermis reveals streaked areas brown in color. These brown-streaked areas are more common on the plantar surface than on the dorsum of the foot.

On sectioning through the center of the toe, the mass is of the same grayish-white color and is streaked throughout by brown to light yellowish lines. This mass measures five and one-half centimetres vertically, eight centimetres anteroposteriorly and six and



one-half centimetres in transverse diameter. The tumor surrounds and displaces the tendon of the extensor digitorum to a more dorsal aspect. The growths extend both below and above the metatarsal bone which is almost completely replaced by this elastic and moderately firm mass. On the dorsal aspect, especially in the distal portion, the mass grows out in a cauliflower-like fashion and covers the uninvolved distal portion of the toe for about one and one-half centimetres.

The articulation, between the proximal portion of the first phalanx and the distal portion of the metatarsal bone, is partially destroyed and replaced by a small mass of brown to brownish-gray tissue measuring ten millimetres vertically and five millimetres anteroposteriorly. Some of this brown-stained tissue has invaded the proximal phalanx for a distance of seven millimetres.

*Microscopic description.*—Sections of tissues studied from the periphery of the tumor mass show that the tumor is well encapsulated by a comparatively dense fibrous connective tissue capsule. From the capsule there extends into the tumor mass trabeculae of fibrous tissue. The trabeculae, in turn, spread out in a fine reticulum and act as a supporting structure to the tumor cells, which are arranged in columns or alveoli. In some areas where degeneration has taken place the connective tissue has undergone hyalinization.

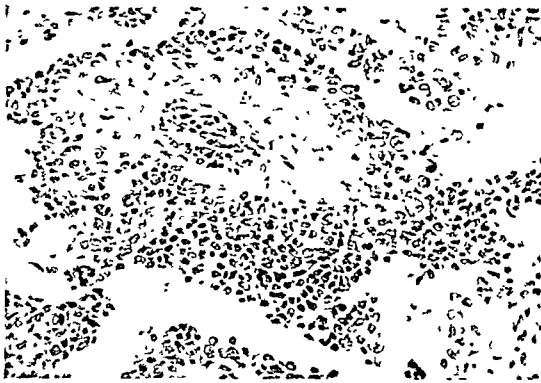


FIG. 3.—Showing the typical oval cuboidal, and polygonal tumor cells. (Mag. 380.)

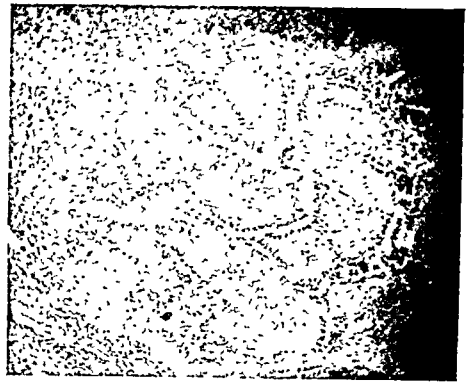


FIG. 4.—Showing tendency of the tumor cells to line clefts. (Mag. 100.)

Throughout the tumor mass there is a variation in the amount of connective tissue present. In some regions the tumor cells are surrounded by large masses of connective tissue and in other regions by only very fine connective tissue strands. The fibrous capsule is well supplied by blood-vessels.

The cellular elements of the tumor consist of a type cell, as well as giant cells, lymphocytes, and pseudoxanthomatous cells.

The type cell is round, oval or cuboidal in shape with a distinct homogeneous, slightly oxyphilic cytoplasm. The nuclei are round or oval and sometimes show small indentations. There is a moderate amount of chromatin with small nucleoli (Fig. 3).

These cells lie singly and are surrounded by fibrous connective tissue. In places there is quite an abundance of intercellular material while in other places the cells tend to line irregular crevices (Fig. 4) or to form alveolar groups in which cell borders cell. The alveolar formation of these type cells occurs especially at the periphery of the tumor, whereas in the central portion near the region where the tumor surrounds and invades the bone, the cells are arranged singly or in column, each column being surrounded by a thin or thick fibrous network.

The giant cells are scanty, irregularly scattered and closely resemble osteoclasts. These giant cells contain many small nuclei, evenly distributed in an oxyphilic homogeneous cytoplasm and are found in the greatest number in places where blood pigment is most abundant especially in the interarticular polyp-like area. (Fig. 5.)

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In close topographic relation to the blood pigment deposits are groups of pseudo-xanthomatous cells. These cells have an irregular, somewhat indefinite cellular margin. The nuclei are small and granular and the cytoplasm is vacuolated. When these sections are stained with Sudan III, a great number of them are found to contain fat droplets and some of these cells contain blood pigment as well. A polariscopic examination of unstained sections revealed the presence of double refractile droplets.

Scattered throughout the tumor, especially in the periphery, are lymphocytes.

In addition to the cells just described there is found quite an abundance of dark yellow-brown pigment, particularly in places exposed to trauma (near the joint). The pigment granules are all found to be intracellular and when stained for iron with potassium ferrocyanide and hydrochloric acid give the Prussian blue reaction. In most instances the pigment granules are distributed along and about the blood-vessels. Recent hæmorrhages are also noticed.

The blood-vessels of this growth are well developed and have a definite adventitial layer. In the centre of the tumor mass close to the bone, the endothelium is quite flattened. The blood-vessels in the periphery of the tumor, however, show swollen endothelial cells. The vessels that lie in the fibrous capsule are surrounded by lymphocytes.



FIG. 5.—Giant cells in relation to blood pigment. (Iron stain.)



FIG. 6.—Showing invasion and destruction of the joint between the metatarsal and phalangeal bones by the tumor mass. (Mag. 8.)

The preëxistence structures such as tendon, bone and cartilage (Fig. 6) are surrounded, invaded and broken up by the tumor mass.

CASE II.—A colored female, seventy years of age, was admitted to the Cook County Hospital January 27, 1930. The tendon sheath tumor, in this case, was an incidental finding at the autopsy (performed by Dr. Philip Shapiro). The post-mortem findings in addition to the tumor mass, which shall be described later, were chiefly those of eccentric hypertrophy of the heart with severe parenchymatous degeneration of the myocardium and brown atrophy: arteriosclerosis and arteriolosclerosis of the kidneys with cloudy swelling; bronchopneumonia of both lower pulmonary lobes; chronic indurated pulmonary tuberculosis at the apex of the left lower lobe with slight bronchiectasis and a huge pedunculated fibromyoma of the fundus uteri.

The tumor of the tendon sheath consisted, grossly, of a large gelatinous, bulbous mass seven centimeters in diameter. It lay over the left first metatarsal space separating, to a fairly wide extent, the great and second toe.

Microscopic studies of sections of the tumor mass revealed it to be composed of the type cells which have been described in the first case, except that they appear to be somewhat smaller in size. These cells are arranged in cords or alveoli and are supported by a fine or heavy stroma of fibrous tissue. Sudan III stain of the tissue shows a moderate amount of fat around the larger blood-vessels of the cutaneous and subcutaneous tissue. The tumor cells themselves contain but only very minute fat droplets.

A careful search was made for giant cells, similar to those found in the first case but without avail. Not a single one could be found. Hæmorrhagic areas or areas of cholesterin deposits were also absent.

Lymphocytes and a few plasma cells are scattered irregularly throughout the tumor mass. The capillary blood-vessels are few in number.

The tumor mass is well separated from the cutaneous and subcutaneous tissue and appears to originate from the tendon sheath. In the basal part of the tumor mass the cells definitely separate the coarse collagen trabeculæ of the tendon proper.

*Discussion.*—In considering the various theories offered as to the histogenesis of the so-called xanthosarcoma, we may say that the tumor is a true neoplasm of mesothelial origin and is not a granuloma for the following reasons. The tumor appears to be derived from the cells that line the tendon sheaths. There is the tendency of the tumor cells to line clefts (Fig. 4), thus imitating the physiologic arrangement of cells from which they have developed. The increase of connective tissue in the tumor mass is due possibly to a transformation of the mesothelial cells to fibroblasts. Such a condition has been very clearly shown by Maximow<sup>10</sup> in cultures of peritoneal exudate containing mesothelial cells. By culturing the peritoneal exudate, he was able to show the transformation of the mesothelial cells into fibroblasts.

It is interesting to note that a malignant form of tumor, simulating to some extent the benign structure of the so-called xanthosarcoma, is described by L. W. Smith<sup>20</sup> as a synovioma. He describes this tumor as characterized by spaces lined in most instances by low cuboidal epithelial-like cells separated by compact cords of spindle-shaped cells which in some portions of the tumor mass are devoid of intercellular substances and fibrils. Mitotic figures are present in both types of cells. He is also of the opinion that both types of cells are derived from a common multipotential cell, since he has shown the synovial lining type and the supporting stromal type with intermediate forms of cells between these two types of cells. He also states that the tumors may arise from the synovial membrane of the joint cavity itself, of the synovial membrane of some overlying bursa, or from the fascial aponeurosis.

Harbitz<sup>14</sup> cites tumors of the auricular capsule and synovial membrane both of which resemble xanthosarcoma. In one case it was a slow-growing tumor with subsequent recurrences upon removal and was more of a sarcomatous nature. In the second case it resembled tuberculosis clinically but histologically it was described as a xanthofibrosarcoma giganteo-cellulare pigmentosum.

Albertini<sup>17</sup> has demonstrated that the ground tissue in his benign xanthomatous giant-cell tumors of the tendon sheath exhibits the structure of mesenchyma.

Unlike McWhorter and Weeks,<sup>21</sup> and others who are of the opinion that these tumors, like the multiple xanthomas, are due to systemic disturbances of the cholesterin metabolism, the deposits of cholesterin in the tumor mass are secondary to the growth of the tumor. Since the pseudoxanthomatous cells are in close topographical relation to pigment deposits of old hæmorrhages, apparently from repeated trauma, the cholesterin deposits are therefore due chiefly to the liberation of cholesterin from the degenerated blood-cells. Beneke,<sup>22</sup> in the report of his case, which deals with a tumor of the foot developing during a course of six years following an injury in which the upper portion of the foot has broken through the skin, also believes that the cholesterin is derived from the degenerated blood, since he finds that cholesterin and hæmosiderin appear simultaneously.

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The fact that cholesterol deposits are secondary to the growth of this tumor mass is further supported by the second case which I have reported. In no place was I able to find cholesterol polariscopically, nor was I able to find old or recent hæmorrhagic areas which would most likely liberate cholesterol to form cholesterol deposits.

In both cases reported the blood cholesterol determination was made. The first case had 147 milligrammes/100 cubic centimetres of blood. The second case had a blood cholesterol of 177 milligrammes/100 cubic centimetres of blood. Both cases then, are practically within normal limits. This finding readily removes the possibility that the tumor growth may have been due to generalized disturbance of cholesterol metabolism or a hypercholesteræmia. Gonzalez Aguilar<sup>23</sup> has also reported a case where, in the absence of a hypercholesteræmia, there were cholesterol lipoids and cholesterol bodies in the tumor mass.

It is shown by Stewart<sup>21</sup> that deposits of cholesterol may occur in various pathological lesions. The cholesterol deposits in the benign tumors of the tendon sheath may be placed, then, in that condition or category in which deposits of cholesterol are due principally to local tissue changes with no chance for the escape of the products of disintegration.

The presence of giant cells has caused a great deal of diverse opinions. Fleissig<sup>9</sup> and others are of the opinion that these giant cells are foreign body giant cells due to the presence of extracellular cholesterol and cholesterol ester deposits. Stewart and Flint,<sup>10</sup> on the other hand, have shown that giant cells were present in the absence of cholesterol deposits in one of the cases they have reported. They believe them to be endothelial in origin.

Mallory<sup>22</sup> states that giant cells of at least two different types occur in tumors. One type results in multiple mitosis and is a true tumor giant cell. It signifies rapid growth and may occur in a variety of tumors. The second type is due to endothelial leucocytes invading the tumor and fusing to form foreign body giant cells.

Broders<sup>4</sup> believes that the function of the giant cells in this tumor mass is to absorb the foreign material present.

Albertini<sup>17</sup> considers the giant cells to be derived from mesenchyma and to be the same as the ground cells except that their protoplasm has not undergone division.

In studying the giant cells in the first case (Fig. 5), one is impressed with the close topographical relationship existing between the giant cells and the hæmorrhagic areas. The giant cells appear to be derived from the endothelium of the blood-vessels and show early attempts to organize the hæmatoma formed by the hæmorrhage. The giant cells then may be considered as a separate entity from the typical tumor cell found in this benign growth of the tendon sheath. This last statement is supported by the studies made on the second case, reported in this paper, where, in the absence of hæmorrhage or hæmorrhagic areas, no giant cells were found.

In view of the fact that these tumor growths are neither malignant nor granulomatous in nature, it would be misleading to call them sarcomatous or granulomatous growths. Therefore, on the basis of microscopical findings, which show that giant cells and xanthomatous cells with cholesterol bodies are occasionally absent, these tumors should be named benign tumors

of the tendon sheath. However, if the giant cells and xanthomatous cells are present, which are secondary to the actual tumor mass, they may be named under Albertini's nomenclature as "benign xanthomatous giant-cell tumors of the tendon sheath."

#### SUMMARY

1. Benign tendon sheath tumors are true neoplasms.
2. Cholesterin deposits are secondary to the tumor growths and are liberated by the degeneration of the red blood-corpuscles.
3. Giant cells are endothelial in origin, and attempt early organization of the hæmatoma formed by hæmorrhage into the tumor substance.

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# VARICOSE VEINS: INDICATIONS AND CONTRAINDICATIONS TO INJECTIONS

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MAJOR complications following the injection treatment of varicose veins are occurring with such frequency, that the call for a voice of warning is imperative. It is unfortunate when such cases are concealed, or divulged under the cloak of confidence. These accidents have been preventable. On the other hand, there are sufferers who are being denied treatment because of timidity based on ignorance. It is not right to deny help to patients for reasons based on prejudice; it is wrong to treat them at a serious hazard.

Buerger's disease (thromboangiitis obliterans) is frequently associated with varicose veins. There is an increase not only in the recognition of cases, but an actual increase in the number of cases occurring. It is an absolute contraindication to the injection treatment. It is easy to see the varicose veins and fail to recognize the early stages of an underlying thromboangiitis obliterans.

Dr. Leo Buerger reports to me a moderately early case of Buerger's disease in which injections of the varicose veins, performed by another physician, were followed at once by gangrene of both legs up into the thigh, necessitating bilateral high amputation!

Preliminary examination must not only include inquiry as to intermittent claudication, but also determine whether there is pulsation in the artery dorsalis pedis and artery tibialis posterior. In doubtful cases Samuels' test should be made, wherein the leg is elevated to an angle of forty-five degrees, and the ankle alternately flexed and extended while blanching of the plantar surface of the foot and pain in the calf are ascertained.<sup>1</sup>

*Elderly Patients.*—Elderly patients are a large group. Men over sixty-five years of age comprise one out of every five male patients entering the clinic at the Los Angeles General Hospital, and one out of every ten of the total number of patients. They contribute the largest number of patients rejected. A vigorous elderly patient in good health may have his varicose veins injected but when to the senility is added some other serious handicap, danger is encountered.

Such an added handicap is senile arteriosclerosis of the legs—evidenced by lack of pulsation in the artery dorsalis pedis and the artery tibialis posterior—that I am strongly opposed to injection of the varicose veins of such patients. In many of these the pain is not due to the veins which are before their eyes, but to the arterial disease which they cannot see. I have had such patients tell me that they must have relief and found on further questioning that the pain was largely in the limb in which there were few,

if any, varicose veins. In the limb with serious varicose veins there may be no pain at all. To occlude the vein in the presence of a gradual occlusion of the artery, is an entirely different story from ligation of the vein in the presence of a sudden occlusion of the artery. The logic and results of occlusion of the vein in the presence of gradual, not sudden, occlusion of the arteries, has been discussed unfavorably by Brooks<sup>2</sup> and by Lipschutz.<sup>3</sup> Aged folk, if their pain is due to the vein, can usually wear a linen-mesh bandage and be comfortable. Often there is impending gangrene of the feet. If gangrene, or phlebitis, or embolism follows treatment, the injection will be blamed.

Mr. F., aged sixty-eight, seen in consultation, had large varicose veins in both legs, containing small thrombotic and calcareous masses. He had severe pyorrhœa so that pus exuded from the gums on the slightest pressure. I refused to countenance the injection treatment of this patient. Two days later he developed a violent acute phlebitis with hyperpyrexia, and, for days, death seemed imminent. If his veins had been traumatized by injection, I believe a fatality would have been inevitable with death laid to the door of the injection treatment. As it was, he recovered, and as frequently happens in this particular type of case, the phlebitis obliterated the varicose veins.

Mrs. B., aged sixty-eight, a patient of Dr. I. W. Lynn, had very large varicose veins of the right leg. The artery dorsalis pedis and artery tibialis posterior had no pulsation. When pressure with the finger on the foot was released, color returned at the site of pressure slowly. There was no other apparent abnormality. Doctor Lynn refused to inject the veins. Just eight days later this patient who had not been injected was seized with a sudden pain in the leg. The great saphenous vein became thrombosed to the upper third of the thigh. The leg turned blue to the knee. Cyanosis deepened. There was no fever but a rapid pulse. Gangrene developed, necessitating high amputation.

Let the reader examine some of these cases with high amputation before his eyes, before he decides he is willing to inject the veins of the patient with absent pulsation in the artery dorsalis pedis and artery tibialis posterior.

I admit that Delater, Jentzer, Paul Linser, and Meisen sometimes allow injection even if there is senile arteriosclerosis in the legs. Reichert<sup>4</sup> has advocated injection for such cases. Delater reports cases to me in which the spasm was relieved by injecting the veins, adding that the effort is futile if the endarteritis is obliterating.

On the other hand, Forestier and Gaugier agree that senile arteriosclerosis of the leg is an absolute contraindication.

Simple debility added to old age may constitute a contraindication. Linser's only fatality was in such a case.<sup>5</sup> Other factors, added to old age, contraindicating injection, may be diabetes or a very high blood-pressure, a history of embolism or thrombosis in coronary or cerebral arteries, or severe focal infection.

*Distant Foci of Infection.*—I have previously warned<sup>5</sup> that phlebitis may be of metastatic origin from infection, acute or chronic, in the pharynx or mouth, and favored the removal of chronically infected tonsils and root abscesses under devital teeth, before injection, lest infection from them,

carried in the blood-stream, set up a phlebitis in veins, traumatized by injection. However, a more liberal position is justified. I was influenced by Gaugier who wrote me two years ago: "After making 300,000 injections we do not believe that infection of the teeth, tonsils, etc., could constitute a contraindication to the sclerosing method. We pay no attention to them." Clinical experience has forced me to Gaugier's position. I have had two cases of phlebitis following injection in which, so far as could be determined, there was no focus of infection. On the other hand, in about four thousand injections in patients who did have foci of infection which were not removed, not a single case of phlebitis developed.

Where there is a past history of phlebitis, not otherwise explained, where there are symptoms of toxic absorption such as rheumatic pain, when the patient is weak or aged—it may be safe to insist upon the elimination of such foci of infection. In other cases their removal is advised but not required. Veins should not be injected while the extraction of teeth is in progress, because at such times when the lymphatic spaces are being torn open there is unusual likelihood of absorption and dissemination of bacteria in the blood-stream. Varicose veins should not be injected in the presence of a subacute pelvic infection, or when the patient has a cold or an acute pharyngitis.

*A Past History of Phlebitis.*—Varicose veins patients with a past history of phlebitis are a large group, comprising one out of every six women and one out of every eight men in my clinic. These patients have veins which cause unusual suffering. I have had a patient declare that he preferred amputation to the continuance of his suffering from varicose veins which followed phlebitis. Should such patients be treated or turned away?

I must answer that each case is an individual problem in surgical judgment. The problem for judgment is not concerned with the question of the patency of the deep veins. That question, while important, is a mechanical problem which must be settled by tests which have been described.<sup>6</sup> The problem for judgment is this: In the individual case, will injection stir up the old phlebitis? This danger merits prolonged thought and study. Mortality from acute phlebitis may run as high as 8 per cent.<sup>6</sup> Even when the phlebitis has been in the superficial veins there may be danger. Hanschell writes me of three cases of recent superficial phlebitis which he injected in which "the resulting phlebitis and periphlebitis was unusually severe and persisted from eighteen months to two years." He who is too indolent to study the principles which I must explain further at some length, should not accept the very heavy responsibility presented by such patients.

How frequently such patients may be accepted and how frequently rejected may be suggested by some case series. I have asked Delater, of Paris, to contribute his results, for he has, I believe, the widest experience in this particular type of case of any worker living. In his series of 131 cases observed there were:



|  |       |
|--|-------|
| Patients with a past history of deep phlebitis.....        | 79    |
| Patients with a past history of superficial phlebitis..... | 52    |
|  | <hr/> |
|  | 131   |
| Patients accepted for injection.....                       | 96    |
| Patients rejected as unsafe.....                           | 35    |
|  | <hr/> |
|  | 131   |

Of the seventy-nine with a past history of deep phlebitis: Patients accepted, forty-four; patients rejected, thirty-five. Of the thirty-five declined, twenty-four had signs of impaired deep circulation. All of the fifty-two cases where the phlebitis had been superficial were treated. All of those treated were cured.

I have a smaller series of forty patients with a past history of phlebitis. Of these there were treated (and with success), twenty-two; rejected, eighteen. Nearly all of my patients had had a deep phlebitis previously.

In deciding whether the patient who has had phlebitis should be taken or rejected, there are four criteria which should enter into the judgment: (1) The time interval since the phlebitis; (2) The question as to whether the phlebitis reached the deep veins; (3) The age of the patient; (4) The possibility of special treatment.

What lapse of time should be allowed after an acute phlebitis before injections are made? The only rule that can be laid down is this: The longer the interval, the less the danger.

Noel Scott<sup>7</sup> waits three months after all inflammation has disappeared. Douthwaite, R. T. Payne,<sup>8</sup> de Takats<sup>9</sup> and J. M. Hayes<sup>10</sup> wait six months. Delater and Troisier wait two years. Hanschell now waits three years. Forestier, previously quoted as waiting ten years, now waits only five years. Gaugier adheres to the position which he took with Sicard, and if the deep veins were involved in a deep phlebitis, advises rejection of the patient even after ten to twenty years, and holds that it may be better for the general practitioner to let them alone entirely. In my opinion, no one should be injected in less than six months after a phlebitis and sometimes I reject patients even after ten years.

The second criterion which distinguishes between a previous superficial phlebitis and a previous deep phlebitis is stressed by Delater, Douthwaite and Gaugier. They hold that there is little or no danger after a superficial phlebitis, but that caution must be used when there has been a deep phlebitis. Payne will never inject when there has been a history of phlegmasia alba dolens. Ronald Thornhill is of the same persuasion.

But how is one to tell now whether a phlebitis in the past did or did not include the deep veins? Tests for the patency of the deep veins now do not tell whether there has been a phlebitis in the deep veins in the past, because some of the deep veins may be shown by patency tests to be open

## INJECTION TREATMENT VARICOSE VEINS

while other deep veins may be occluded and harbor bacteria. Deep veins once thrombosed by infection may be recanalized and now be patent.

The following items do give warning that a previous phlebitis was deep: A history of surgical trauma in the lower abdomen before the phlebitis (Delater); trouble in walking for two months after phlebitis (Delater); past recurrences of the phlebitis (Delater); œdema one-third of the way up the leg (Douthwaite); a white œdema (Gaugier); hydro-arthritis of the knee (Gaugier).

In a superficial phlebitis, the inflammation is localized at the painful area, the recovery is rapid, and if there is a remaining œdema of the lower leg it disappears after application of an Unna's paste bandage (Delater).\*

Forestier dissents. He minimizes the importance of the distinction between a previous superficial phlebitis and a deep phlebitis; so do Meisen and McPheeters.<sup>11</sup>

Both parties in this controversy have truth behind them: Happy results from injection by careful men are being obtained in cases where the previous phlebitis was deep. Nevertheless, special caution in treatment, to be described below, is essential when there has been a history of deep phlebitis.

A third criterion which I consider important is the age of the patient. A young patient with a history of phlebitis may be accepted while an elderly patient is refused because younger patients have better resistance to infection and are not such likely subjects for thrombosis and embolism.

*Special Treatment in Patients with a Past History of Phlebitis.*—Some of the patients who have had phlebitis demand very different treatment from ordinary cases. In such cases instead of the usual ambulatory treatment, some of these patients are hospitalized and ordered to stay in bed. This is simply the old surgical principle of preventing the dissemination of infection by putting the part to rest. The veins are further splinted by the application of a firm linen-mesh bandage all the way up the leg, which is worn day and night. These patients require only one-tenth as large doses as ordinary patients. One or two minims of the quinine urethane solution is used as the first dose. After injection they suffer pain, not experienced by other patients, but this pain is relieved at once as long as the leg is kept bandaged.

*Conclusion.*—For the protection of the patient, it is recommended that before any injection treatments there be a complete physical examination or that as a minimum the following items of history and physical examination be ascertained:

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\* Deutsch, H., maintains that a deep phlebitis always begins with a sudden pain in the calf muscles—Zur behandlung der akuten lokalisierten phlebitis der unteren extremität, Wien. klin. Wchnschr., vol. xlii, p. 1162, September 5, 1929. Ipsen, J., notes that a thermometer on the plantar surface of the foot shows fever in a deep phlebitis but no fever in a superficial phlebitis—Recherches sur les artères à l'état pathologique, Acta chir. Scand, vol. lxxv, p. 341, 1929.

*History*

Name .....  
 Address .....  
 Age ... ..  
 Age when varicose veins began.....  
 .....  
 Pain.....For how long  
 .....  
 Inflammation in leg.....  
 Phlebitis or milk leg.....  
 When .....  
 Typhoid..... When.....  
 Pelvic troubles.....  
 Intermittent claudication.....  
 .....  
 Has patient ever taken quinine with symp-  
 toms of toxæmia.....

*Physical Examination*

Temperature..... Pulse.....  
 Blood-pressure .....  
 Do veins extend above the inguinal region  
 on the abdomen.....  
 Œdema of leg.....  
 Pulsation of artery dorsalis pedis.....  
 .....  
 of tibialis posterior.....  
 Cyanosis or rubor when foot is dependent  
 .....  
 Pain or blanching of toes when leg is ele-  
 vated and ankle is alternately flexed and  
 extended .....  
 Sclerosis in veins.....  
 Pain on walking five minutes with legs  
 firmly bandaged.....  
 Description of veins.....  
 Pelvic tumors.....  
 Pelvic Infection.....

Urine: Specific gravity.....albumen..... sugar.....

In this study I am especially indebted to the following workers who have generously contributed material, largely unpublished: *Paul Linser*, of Tubingen; *Nobl*, of Vienna; *Jentzer*, of Geneva; *Age Berntsen*, and *V. Meisen*, of Copenhagen; *Delater*, *Forestier*, *Gaugier*, and *Troisier*, of Paris; *Douthwaite*, *Hanschell*, and *Treves-Barbour*, of London; *Leo Buerger*, of Los Angeles.

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- <sup>11</sup> McPheeters, H. O.: Varicose Veins, p. 102, F. A. Davis Co., 1930.

# SOLUTION OF DEXTROSE AND SODIUM CHLORIDE FOR OBLITERATING VARICOSE VEINS\*

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EIGHTEEN months have now elapsed since we began the injection treatment of varicose veins at the Johns Hopkins Hospital out-patient department and 464 cases have been completed. Since the publication of our original article,<sup>1</sup> some changes have been made in technic and sufficient time has elapsed to allow us to make a fair estimate of the worth of this form of

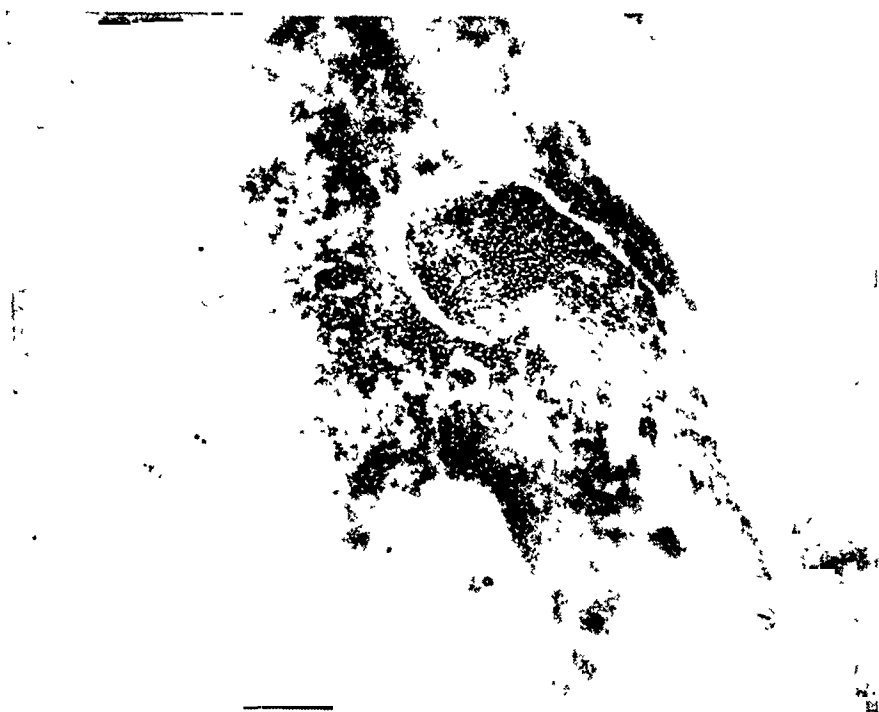


FIG. 1.—Showing the appearance of the abdominal wall of a dog one week after the subcutaneous injection of 6 cubic centimetres of a solution of equal parts of 50 per cent. dextrose and 30 per cent. sodium chloride in the area marked "2", and two weeks after the injection of the same amount of solution in area marked "1." Two distinct hard masses were palpable. Skin is intact.

treatment. Furthermore, there are several points in our first article which we feel require greater emphasis and some explanation.

*Experimental.*—Concomitantly with our clinical work we began a series of injections into the external jugular veins of dogs.<sup>1</sup>

The vessels were thrombosed with solutions of sodium chloride 20 to 30 per cent.: sodium chloride 30 per cent. plus equal parts of dextrose 50 per cent.; sodium salicylate 20 per cent. Specimens of the injected veins were removed forty-eight hours, seventy-two hours, one week, two weeks, and four weeks following injections and microscopic studies made. The forty-eight-hour specimens showed a large thrombus obliterating the

\* This investigation has been carried out in the Division of Plastic Surgery in the Johns Hopkins Hospital and in the Hunterian Laboratory.

lumen of the vein and a complete destruction of the endothelial lining. There was a leucocytic infiltration of the media and adventitia. At the end of a week all signs of acute inflammation had disappeared and there was definite evidence of beginning organization of the thrombus. Organization of the thrombus was progressive and almost complete at the end of four weeks. The smooth muscle of the media coat of the vein had been replaced, in part, by fibrous tissue. The external jugular veins of twenty-eight dogs were used for experimental purposes and in spite of the fact that thrombi were formed in veins very close to the heart, with a swift blood-current and considerable negative pressure there was in no case evidence of migration of the thrombus.

*History and examination of patient.*—A careful vascular history and examination should precede the injection treatment of each case. For this purpose we devised a simple chart<sup>1</sup> which upon completion gives sufficient data to determine in the majority of cases whether the individual is a fit

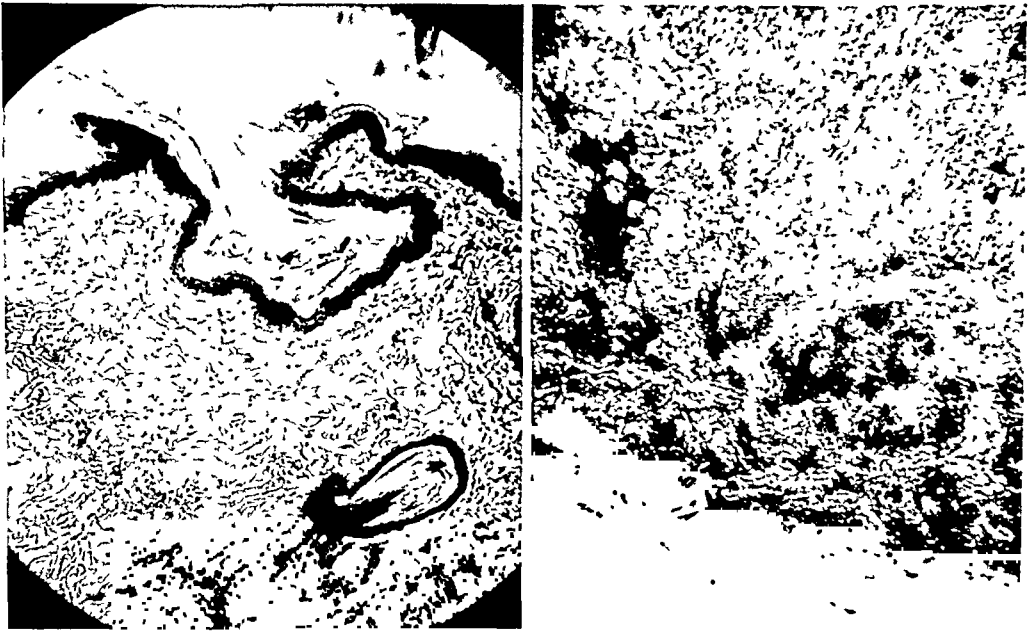


FIG 2—Low power photomicrographs of sections of skin and subcutaneous tissue taken from area marked "I" in FIG 1. The skin and subcutaneous tissue show marked edema but no cellular destruction. There is tremendous leucocytic infiltration in the fat.

subject for this treatment. We have adhered strictly to this outline and feel that it has saved us from having any serious untoward results.

*History.*—The duration, etiology, progress and symptoms of the varicosities are determined.

A general medical examination is made in special cases. It is usually indicated by the patient's age or certain findings in the regional examination which make one suspicious of some organic disease either associated with or a causative factor of the varicosities. If such is the case, injection is contra-indicated. If in the examination of the varicosities active or latent phlebitis is evidenced by the presence of thrombosed segments or tenderness, one should wait at least a year before giving injections.

Perhaps the most important contra-indication is obstruction to the deep

## OBLITERATIVE VARICOSE VEINS

veins. This is determined from the history and is suggested by the presence of œdema and a thickened shiny tight skin. We do not feel that there is any absolute test for determining the degree of patency of the deep veins once they have been thrombosed, and in many cases are convinced that where there has apparently occurred complete restoration of function any interference would upset the circulatory balance. Only in the presence of an ulcer which will not heal by supportive measures is one justified in obliterating the superficial varicosities. The absence of arterial pulsations in the extremities, due to arteriosclerosis, Beurger's or Raynaud's disease further contra-indicates treatment.

It is our feeling that better results will be obtained if the veins of pregnant



FIG. 3.—Cross-section of external jugular vein of dog, removed seventy-two hours after injection with  $7\frac{1}{2}$  minims (0.45 cubic centimetres) of 50 per cent. dextrose and 30 per cent. sodium chloride, equal parts, seen under low power. Section shows entire vein occluded by a firm thrombus. The endothelium is not visible. Media and adventitia show slight inflammatory reaction as evidenced by leukocytic infiltration and dilatation of the vasa vasorum.

women are injected several months after delivery. Only in the presence of an ulcer is treatment given during pregnancy.

*Solutions.*—With the increasing popularity of this relatively new treatment of varicose veins the number of individuals doing injections has also increased. The solutions used by operators are more or less determined by the convenience with which they can be obtained.

In the early days of our clinic we sought a solution which would be non-toxic, effectual in the majority of cases with a minimum amount of reaction (*i.e.*, cramp) and one which would not cause a slough if a moderate

amount were injected outside of the vein. Experimentally we found that a mixture of equal parts of 50 per cent. dextrose and 30 per cent. sodium chloride made an ideal solution. (One hundred cubic centimetres of such a mixture contains twenty-five grams of dextrose and fifteen grams of sodium chloride.) When injected into the abdominal wall of a dog, intradermally (in amounts up to one cubic centimetre) subcutaneously or intramuscularly (in amounts up to six cubic centimetres) no slough resulted. However, there was a marked inflammatory reaction which could be lessened if active massage was instituted over the area immediately after injection. Experimentally and clinically the solution causes an endophlebitis equal to that of the salt solution alone and the resulting thrombus is exceedingly firm.

In the course of doing human injections a careful operator could hardly deposit more than a few drops of the solution in the skin or six cubic centimetres subcutaneously without seeing the swelling of the tissues or being notified by the patient that he was having pain or burning at the site of injection. We have inadvertently injected varying amounts of this solution outside of the vessel wall no less than 100 times in the course of 2500 injections. Just how much of the solution has been injected into the tissues at any one time we have no way of estimating because we always stopped the injection the moment a patient complained, but in our hands this mixture has never caused a slough comparable in any manner to those we have seen resulting from the use of sodium chloride, sodium salicylate or quinine. In this respect there were but two accidents following the use of dextrose-sodium chloride solution which we feel should be reported.

In one case a faulty injection of ten cubic centimetres of solution was made on the inner aspect of the knee-joint by an inexperienced worker. The patient complained of severe pain and burning and the area was actively massaged. After about thirty minutes the patient left the clinic. Forty-eight hours later when he returned for observation there was a mass on the inner aspect of the knee about the size of a small saucer, the tissues were flaming red, indurated, hot and very tender. The patient said that he had had considerable pain but had never ceased his work as "setter up" in a bowling alley. Hot compresses and rest were advised. Several days later a thin sero-purulent discharge appeared at the site of the needle puncture. With a sharp pointed applicator this tiny opening was dilated to permit freer drainage. The skin did not slough, and the inflammation subsided completely in about three weeks' time. We are of the opinion that in this case almost the entire ten cubic centimetres of solution was injected into the tissues and that fat necrosis followed.

The other accident occurred in a varix the overlying skin of which was so thin that the vein was on the point of rupture. The varix was injected and well thrombosed on the next visit of the patient to the clinic. Six days later the skin ruptured and the thrombus was extruded. No hæmorrhage occurred. The exposed vessel was curetted and the wound granulated. Healing was complete in four weeks.

The cramp following the injection of dextrose-salt solution is much less severe than that following sodium chloride alone or sodium salicylate and about the same as that following 75 per cent. invertose. Benzyl alcohol (1.5 grams to 100 cubic centimetres) added to the mixture of dextrose and

salt solution acts as a preservative and diminishes the cramp by virtue of its anæsthetic property.

The action of the solution is rapid and the thrombosed vessels can often be palpated within four to five minutes following injection. With the exception of four cases we have not had to resort to other solutions in order to produce thrombosis. In these cases quinine hydrochloride plus ethyl urethane was used with rapid results. However, these patients complained of pain and tenderness in the legs for many weeks. Fifty injections were made with 75 per cent. invertose. Its use was discontinued following two very severe reactions. In both instances the symptoms were identical. About three minutes after the injection of eight cubic centimetres of this solution the patient complained of excruciating pain across the sacrum, pain down the arms, and a general peculiar feeling all over the body. In one instance the pain across the back was so severe that the patient was unable to move and had to lie in a semi-prone position for about ten minutes. However there were no after effects.

We have endeavored to use 50 per cent. glucose alone with tourniquets and vein occluders but our results have not been satisfactory.

*Preparation of dextrose-sodium chloride.*—The 50 per cent. dextrose and 30 per cent. salt solutions may be prepared in separate flasks and autoclaved for twenty minutes under twenty pounds pressure. This method of sterilization often results in carmelization of the dextrose. It is perhaps better to boil the solutions over a very low flame or water bath for ten minutes.

At the time of use the two solutions may be mixed in any desired proportion. For the general run of cases the mixture of equal parts has proven satisfactory. However in very thin-walled vessels and telangiectasis two parts of glucose may be added to one part of salt. The solutions should be very thoroughly and carefully mixed before filling the syringe in order that the buffer action of glucose may be obtained. If this is not done the chances for a slough are accentuated if a faulty injection is done. To insure thorough mixing it is our custom to measure equal parts of the solutions in a graduated medicine glass and with the syringe aspirate and eject the solution with force several times just before use.

*Dosage.*—The amount varies from one to ten cubic centimetres depending on the varix to be injected and also on the individual patient. It is advisable that a single initial injection be given in any case and that the dose be small in order that the patient's reaction may be determined. It is our routine to inject no more than ten cubic centimetres in a single varix and not over twenty cubic centimetres at one sitting. However, we recently learned that one investigator injected seventeen varices with eighty-four cubic centimetres of this solution at one time without any untoward results. This may be a perfectly safe procedure but we doubt its wisdom.

If the dosage is properly graduated the thrombosed veins are only slightly tender and the patient suffers no discomfort. Rarely do we see a periphlebitis and when it does occur it is usually in very fair-skinned people.



It has been our observation that the vessels in patients of the brunette type and the negro are more resistant to sclerosing solutions.

*Technic.*—A twenty-six guage, five-eighths inch, short bevel needle can be used for all sized varices. This type needle permits a very little spring and can be inserted with practically no discomfort to the patient. The ordinary five or ten cubic centimetres glass syringe is easier to handle than the lock syringe.

*Site of injection.*—As a general rule the injection is usually begun distally and successive injections made higher up according to the manner in which the vessels thrombose. As we stated before,<sup>1</sup> in those cases which there



FIG. 4.—Illustrating a case of marked varicosities above and below the knee of both legs before and after treatment of twenty injections of a mixture of equal parts of 50 per cent. dextrose and 30 per cent. sodium chloride were given. Treatment not completed. A—taken March 22, 1930. B—taken April 24, 1930.

are varices above and below the knee an attempt is made to block the main channel just below the knee. After this is accomplished the varices distally situated respond more quickly to treatment. We are convinced that the entire affected venous tree must be injected and obliterated to prevent the formation of new varices or the opening up of those previously obliterated. We have thrombosed vessels in the upper third of the thigh without untoward results.

In those cases where there are varices present below the knee, and the internal saphenous vein is not varicose but dilated, and stands out like a whip

cord from the fossa ovalis down to the knee, we feel that the injection treatment should follow the ligation, and resection of a portion of this vessel in the upper third of the thigh.<sup>2</sup> This is distinctly a hospital procedure and the patient should be confined to bed for no less than three days following the operation. This procedure will help to prevent the recanalization of the thrombosed vessels as well as the formation of new varices.

*Procedure.*—It has been rather well established that the horizontal position of the leg is one of choice both for the patient and the operator during the injection.

While the patient is in the standing position the varices to be injected are traced out on the skin with mercurochrome.<sup>3</sup> The ordinary toothpick applicator is used for this purpose. The patient is then asked to lie down and tourniquets are applied two to three inches below and above the proposed

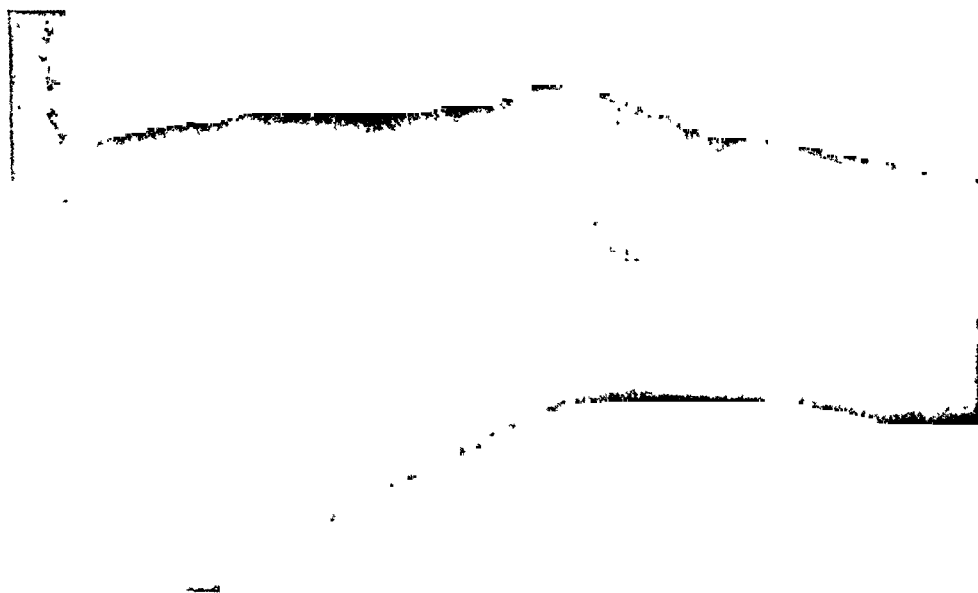


FIG. 5.—Plain X-ray, lateral view of left leg in FIG. 4 taken after large vessels above and at the knee had been thrombosed. The rather dense shadows cast by the thrombosed veins are plainly seen, thus illustrating the firm dense thrombus resulting from the injection of the mixture of sodium chloride and glucose.

site of injection. If the varix to be injected is very large the leg is first elevated above the patient's head to drain the varix of blood before the tourniquets are applied. The vessels are now in a collapsed state and the operator can be sure that the injected solution will have an opportunity to come into intimate contact with the vessel-wall. The injection area is then cleaned with alcohol and the injection slowly and carefully made. Alternately aspirating a few drops of blood with each one or two cubic centimetres of fluid injected.

The tourniquets are allowed to remain on for three to five minutes following injection during which time the varix is gently stroked to distribute the solution. Leakage will seldom occur from the puncture wound. However it is perhaps safer to make pressure with a gauze pledget and adhesive strap. The patients are allowed to rest in the prone position for five to ten minutes longer. A full-length pressure bandage is then applied to the leg

and worn by the patient continuously during treatment and for three weeks after the last injection. This reduces the size of the thrombus, insures support to the thrombosed and inflamed veins during the period of organization and minimizes the chances of canalization. Furthermore, the bandage greatly adds to the comfort of the patient during this period. The success of an injection depends upon the operator's ability to bring the irritating solution diluted with a minimum amount of blood into contact with the vessel-wall, and hold it within a limited area for a long enough time to destroy the endothelial cells. If these two conditions can be satisfied a very weak solution like 50 per cent. glucose alone may be used, if they cannot the more irritating solutions whose action is more rapid must be resorted to. This is often demonstrated in the same patient, as the large tortuous vessels with thickened walls will respond immediately to injection because the blood-current is sluggish and can be controlled, whereas the smaller thin-walled veins require many injections of the same solution because the current is swift and cannot be controlled with tourniquets or vein occluders, and the solution is washed away into the general circulation before it has opportunity to act.

*Complications.*—Immediately following the use of 30 per cent. sodium chloride alone there were three superficial ulcerations due to leakage from the needle hole and three patients developed an ascending chemical phlebitis with thrombosis of the internal saphenous vein up to the sapheno femoral opening. These complications occurred in the very early days of the clinic and we have since abandoned the use of sodium chloride alone. There were two severe reactions after the injection of 75 per cent. invertose which were reported in detail above. Although only four patients were given supplementary injections of 10 per cent. quinine solution they all complained of severe pain in the thrombosed vessels forty-eight hours later and almost continuous discomfort in the legs for about four weeks in spite of all palliative measures. Following the use of the mixture of glucose and salt solution which we have employed almost exclusively in the treatment of 400 cases, there were but two local accidents; one, as previously mentioned, a very severe inflammatory reaction following the injection of a large amount (ten cubic centimetres) of solution into the tissues, and the other, a rupture of a very thin-walled varix. Five patients had a marked periphlebitis following the injection of too much solution in a single varix. This condition occurred in each instance on the thigh and cleared up in about two weeks' time. One patient developed an infectious phlebitis in a varix thrombosed two months previously. On examination the varix was red, very tender and hard. Cold applications were applied and the inflammation promptly subsided. Brownish pigmentation of the skin rarely occurs following the use of this solution. There has been no case of embolism.

*Results.*—As is true with any surgical procedure, the results will not be perfectly satisfactory in every case. In our experience patients with the most marked varicosities and definite symptoms are those who receive the most satisfactory results. Even after the first few injections they are relieved of cramps in the legs and the accompanying heavy, tired feeling.

Quite often there is a history of marked pain in the varicosities of the leg during the first few days of menstruation, at times so severe as to compel the individual to stay in bed. The majority of patients with this symptom have been cured, although a small percentage are unrelieved even though all visible and palpable varicosities have been obliterated.

Perhaps the most trying cases are those patients who have no symptoms and desire treatment for cosmetic reasons only. No matter what the previous condition of the legs might have been and how good the result may be as far as obliteration is concerned they are rarely entirely satisfied.

The cases complicated by ulcer formation have responded promptly and satisfactorily to treatment where it has been possible to thrombose the offending varix. Of twenty-one such cases treated but two have had recurrences. One developed a fresh ulcer eight months after treatment, and the other had a recurrence in the same place ten months after treatment with recurrence of the varices.

The treatment of eczemas has not been so satisfactory. About 50 per cent. of these have been cured, the remainder have been improved.

*Recurrences.*—Patients are routinely requested to wear bandages for three weeks following the last injection, then to go without support for one week and report for observation. It is frequently found necessary to obliterate one or two small varices which have enlarged or were obscured by the tight bandages. The patients are then requested to return two months later for further observation. Very few of the clinic patients have returned at this time, and those that did had a reopening of the obliterated varices. We can only conclude that those patients who did not return have received satisfactory results.

We have classified as recurrences those cases which did not receive a permanent obliteration of the injected veins following the one-month period. Sufficient time has not elapsed to determine whether these patients will develop new varices.

One hundred cases have been accurately followed, the oldest cure being eighteen months and the youngest six months. In this group there were ten patients who returned for further treatment and are considered recurrences (10 per cent.). They all occurred within the first four months after treatment, several after six weeks. In as much as the great majority of the obliterated vessels has been converted into scar tissue and almost completely absorbed in six months' time, we believe one can safely conclude that reopening will seldom occur after this period.

Six of the recurrences were only partial and only a few injections were required to re-obliterate the varices. Strange to say these patients had rather small isolated varices confined to the leg. In four cases recurrence was almost complete. Of these patients one had four small varicosities below the knee, while three had tremendous varicosities both above and below the knee. The varicosities below the knee remained obliterated while those above recurred. We are of the opinion that the recurrences in seven of these cases were due to incomplete thrombosis, and that the lumina of the veins were

at no time completely obliterated but were occupied by mural thrombi. Very often in our experimental work injected veins were removed and found to be incompletely thrombosed due to the fact that there had been only partial destruction of the intima. For this reason we gently massage the vessels after injection in an attempt to bring the solution into contact with the entire vessel-wall. In three of the cases where the varicosities were on the thigh, no doubt canalization of the thrombi occurred from the back pressure of the heavy column of blood. This was clearly illustrated in the case of a young woman thirty-two years of age who became pregnant one month following discharge. She stated that the veins began to grow prominent again about the third month of pregnancy and became steadily worse. She returned for treatment and the veins have been re-injected and thrombosed without difficulty. Were it possible to devise some tight support that could be worn on the thigh for several months following obliteration of the varices until the thrombi had become completely organized the chances of canalization would be greatly diminished. Constant application of adhesive straps is not well borne by the skin and elastic stockings are expensive and not entirely satisfactory. Whether resection of a portion of the internal saphenous in the middle third of the thigh will prevent this recurrence is yet to be determined and the procedure is not without considerable danger of embolism.

#### SUMMARY

1. Experimental injections of solutions were made into the external jugular veins of twenty-eight dogs. In no case was there migration of the resulting thrombus.

2. A brief outline of the history and physical examination of varicose vein patients is given together with the contra-indications to injection treatment.

3. The mixture of 50 per cent. dextrose and 30 per cent. sodium chloride as an injection solution is discussed. A detailed report of the preparation, mixing dosage, and technic of injecting the solution is made.

4. Four hundred and sixty-four cases have been completed in which dextrose sodium chloride solution was used almost exclusively. There were but two complications of any consequence following the injection of this solution.

5. A careful follow-up in 100 cases shows a 10 per cent. recurrence of the old varices, in 7 per cent. of the cases the recurrence was partial; in 3 per cent. almost complete. Recurrences are early and are believed to be due to incomplete thrombosis in the majority of cases.

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# THE RELATION OF CALCIUM TO THE HÆMORRHAGIC TENDENCY IN OBSTRUCTIVE JAUNDICE

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THE hæmorrhagic tendency complicating certain cases of obstructive jaundice has long been recognized. For the past twenty years, this bleeding tendency has been considered by most authorities to be related closely with the availability of calcium in the blood-stream for the production of clot formation. The exact mechanism, however, in which obstructive jaundice interferes with the availability of the blood calcium is not well understood.

The bleeding tendency may become so marked that it leads to the patient's death. On account of this, certain measures have been advocated to correct this hæmorrhagic tendency, prior to operation. One of the most common procedures is the intravenous introduction of calcium in the form of calcium chloride or some other soluble calcium salt. Lee and Vincent<sup>1</sup> in 1915 were the first to advocate this form of treatment, and later Walters<sup>2</sup> and Whipple<sup>3</sup> popularized it. The usual procedure, as advocated by Walters, consists of daily injections of five cubic centimetres each of a 10 per cent. solution of calcium chloride for three days just prior to operation. This form of treatment has been carried out on many patients with obstructive jaundice, operated upon at the Massachusetts General Hospital. However, in many of these cases it has not proven efficacious for the prevention of post-operative hæmorrhage. Because of this fact, a critical study has been made of the relation calcium bears to the coagulation of the blood in obstructive jaundice.

*The Relation of Calcium to the Coagulation of Blood.*—"In vitro" the rôle that calcium plays in the coagulation of normal blood is readily demonstrated by precipitating the calcium from the blood with a soluble oxalate salt, such as potassium oxalate, or by the addition of sodium citrate, in which case the calcium is bound to the citrate radicle and is no longer present in a utilizable form. Interference with the solubility and the ionization of the calcium by either of these methods prevents the blood from coagulating. Accordingly, the generally accepted theory is that calcium in a soluble and partially ionizable form is necessary for the coagulation of the blood.

Normal blood coagulates in six to twelve minutes, when the multiple tube method described by Lee and White<sup>4</sup> is employed. The blood from patients with obstructive jaundice not uncommonly requires twenty to thirty minutes, or even longer, to coagulate by the same method. This lowered coagulability of the blood, as evidenced "in vitro," has been considered to

be due to a union of the blood calcium with bile circulating in the blood which rendered the calcium unavailable for the clotting of the blood.

This theory has never been proven. King and Stewart<sup>5</sup> in 1909 were the first to hint at the possible advantages of calcium therapy in jaundiced patients. From their studies they concluded, "The bile pigments circulating in the blood in obstructive jaundice gradually absorb the available calcium of the organs and tissues to form calcium compounds." They thought that this was possibly a mechanism to protect the body against the deleterious effects of the bile circulating in the blood. They based this on the fact that, in their experiments on obstructive jaundice, they found an increase of 16 to 20 per cent. in the circulating blood calcium. However, more recent investigations by others have shown the blood calcium to be essentially normal in cases of obstructive jaundice.

King, Bigelow and Pearce<sup>6</sup> in 1911 came to the same conclusion as King and Stewart. They were the first to suggest that the decreased coagulability of the blood in obstructive jaundice might be due to the fact that the calcium is bound to the biliary pigments in such a way as to be unavailable for the process of coagulation.

Later, Lee and Vincent<sup>7</sup> in 1915 were the first to advocate the use of calcium salts in the pre-operative preparation of jaundiced patients for the prevention of post-operative hæmorrhage. They advocated the use of the calcium "in vitro" test, and showed that the addition "in vitro" of calcium chloride to the blood from patients with obstructive jaundice increased the coagulability of it. This was the first direct evidence which indicated that there might be a deficiency in the available calcium. Here again, however, this test does not hold true in the majority of cases, as will be shown later in this paper. Lee and Vincent advocated calcium lactate by mouth, and also stated if a more prompt effect were desired, a soluble calcium salt could be given intravenously.

Following this report, Walters<sup>8</sup> in 1921 popularized the use of calcium chloride intravenously as a pre-operative measure in jaundiced patients. He reported a reduction in the mortality rate from post-operative hæmorrhage, in cases which received this form of treatment. Whipple<sup>9</sup> in the same year recommended the use of pre-operative intravenous infusion of a 0.2 per cent. calcium lactate solution to prevent post-operative oozing.

*Blood Calcium in Obstructive Jaundice.*—If the theory is correct that the blood calcium combines with the bile pigments to make them relatively non-toxic and at the same time this union renders the calcium unavailable for the clotting of blood, then one should find an increase in the blood calcium in obstructive jaundice, proportional to the degree of jaundice; or a decrease in it, if one assumes the calcium is excreted along with the bile pigments. Accordingly, the blood-calcium level was investigated in a series of animals, in which obstructive jaundice had been produced by ligation and division of the common bile duct. Cats were used in this investigative work. All the animals rapidly developed marked jaundice. The degree of jaundice was followed with the quantitative van den Bergh test which indicates the number of milligrams of bilirubin per 100 cubic centimetres of serum. The animals lived a maximum of three to four weeks.

Calcium determinations were made before the jaundice was produced and repeated at intervals after ligation of the common bile duct, until the animal's death. These are shown in Table I. The Tisdall<sup>7</sup> modification of the Kramer-Tisdall method was used for the calcium determinations. The normal blood calcium in cats was found to be essentially the same as in

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human blood. This is considered to be in the neighborhood of 9.0-11.0 milligrams of calcium per 100 cubic centimetres of serum. Some of the figures reported here are a little high, but not enough to interfere with the conclusions to be drawn from them.

TABLE I  
*Serum Calcium Values in Experimental Obstructive Jaundice*

| Animal | Pre-operative |            |          |           | Post-operative |           |          |           |   |
|--------|---------------|------------|----------|-----------|----------------|-----------|----------|-----------|---|
|        | Cal-cium†     | Janu-dice‡ | 10th Day |           | 15th Day       |           | 20th Day |           |   |
|        |               |            | Cal-cium | Jaun-dice | Cal-cium       | Jaun-dice | Cal-cium | Jaun-dice |   |
| 60     | 10.4          | 0          | ....     | ....      | 10.2           | 8.2       | 9.5      | 10.0      | Death twenty-eighth day post-operative from hæmopericardium following cardiac puncture. |
| 62     | ....          | 0          | 11.0     | 11.6      | 12.0           | 28.5      | 10.8     | ....      | Death twenty-eighth day post-operative.   |
| 63     | 10.5          | 0          | 9.5      | 9.8       | ....           | ....      | ....     | ....      | Death seventeenth day post-operative from ether.  |
| 67     | 12.1          | 0          | 11.0*    | 10.0*     | ....           | ....      | ....     | ....      | Killed fifth day post-operative because wound was septic.                               |
| 69     | 12.4          | 0          | 11.6     | 15.0      | ....           | ....      | ....     | ....      | Death twelfth day post-operative from cardiac puncture with hemopericardium.            |
| 79     | 11.6          | 0          | 11.2     | ....      | ....           | ....      | 13.2     | 12.4      | Death on twenty-sixth day post-operative.   |

\* These figures were from blood taken on the fifth day post-operatively.

† Calcium figures are expressed in milligrams of calcium per 100 cubic centimetres of serum.

‡ Jaundice is expressed in milligrams of Bilirubin per 100 cubic centimetres of serum in all tables.

Following the development of the jaundice which became marked in a few days, there was practically no change in the blood-calcium level. In two instances, animals 60 and 79, figures as high as 13.0 milligrams were obtained. I think these were probably due to errors in technic. Thus in animal 60 the blood-calcium level the day before was 9.5 milligrams. The remainder of the figures varied from 9.5 milligrams to 12.0 milligrams. These are within the range of the calcium level in six normal cats, which varied from 10.4 milligrams to 12.4 milligrams. From these experiments the conclusion to be drawn is that obstructive jaundice of a marked degree in cats, lasting as long as three weeks, does not affect the blood-calcium level. There is neither an accumulation of it along with the bile pigments nor is there a diminution of it due to an increased excretion of it.

Similar determinations were made on a series of patients with obstructive jaundice. Table II gives the results in this group. These patients were all operated upon. Some of them developed post-operative hæmorrhage, but even in these the blood-calcium level remained normal. Case 6 had the lowest figure, which was 7.2 milligrams, but this represented the calcium level of the plasma instead of the serum. In Case 3 the calcium level was 8.8 milligrams, which is practically normal, despite obstructive jaundice of twelve months' duration.

In Table III I have tabulated serum calcium levels reported by a number



of other investigators. All the figures, both experimental and clinical, except those reported by Buchbinder and Kern<sup>12</sup> in their experimental studies in puppies with obstructive jaundice, and those in three cases, reported by Kirk and King,<sup>8</sup> are essentially the same as I have reported.

A reduction of the blood-calcium level to 5-7 milligrams per 100 cubic centimetres of plasma produces signs of tetany, according to Sollman.<sup>13</sup> Despite this decrease in blood calcium, no interference of the coagulability

TABLE II  
*Serum Calcium Values in Jaundiced Patients*

| Case | Diagnosis   | Duration of Jaundice | Degree of Jaundice | Calcium       |
|------|---|----------------------|--------------------|---------------|
| 1.   | Cholelithiasis with stone in the Common Bile Duct.....                  | 2 weeks              | 7.0                | 10.4          |
| 2.   | Carcinoma of Pancreas with Obstructive Jaundice.....                    | 6 weeks              | 24.0               | 10.4 and 9.5  |
| 3.   | Carcinoma of Pancreas with Obstructive Jaundice.....                    | 12 months            | 16.0               | 8.8           |
| 4.   | Carcinoma of Pancreas with Obstructive Jaundice.....                    | 2 weeks              | 16.0               | 11.0          |
| 5.   | Post-operative Stricture of the Common Bile Duct.....                   | 3 months             | 21.0               | 9.0           |
| 6.   | Carcinoma of Biliary Passages with Obstructive Jaundice.....            | 2 weeks              | 18.75              | 7.2*          |
| 7.   | Carcinoma of Pancreas with Obstructive Jaundice and Cholelithiasis..... | 12 days              | 21.0               | 11.4 and 10.3 |
| 8.   | Carcinoma of Pancreas with Obstructive Jaundice.....                    | 2½ weeks             | 18.0               | 10.3          |
| 9.   | Cholelithiasis with Stone in Common Bile Duct.....                      | 2 weeks              | 16.0               | 10.9 and 10.5 |

\* This was determined from plasma instead of serum.

of the blood in these cases has ever been noted. Simpson and Rasmussen<sup>14</sup> found no decrease in the coagulability of the blood in the thyroparathyroid-ectomized animals in which tetany was produced. In the cases of obstructive jaundice I have studied, the blood-calcium level was never diminished sufficiently to produce signs of tetany, which indicates that there was sufficient calcium in the blood for purposes of coagulation.

Zimmerman<sup>11</sup> in 1927 brought forward some important evidence to show that the diminished coagulability is not due to a lack of calcium in the blood. He was able by the use of parathormone to increase the blood calcium to double the normal value in cases of obstructive jaundice. Despite this great increase in the circulating blood calcium he found no increase in the coagulability of the blood in obstructive jaundice.

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Further proof that in obstructive jaundice there is sufficient calcium for the coagulation of blood is brought forward by Kirk and King.<sup>8</sup> They used an ultra-filtration method for determining the diffusible calcium in the blood and came to the conclusion that the percentage of ultrafilterable calcium found in the blood in obstructive jaundice was below that in normal blood, but the difference was not sufficiently great to account for the frequent delayed coagulation time in jaundice.

*The Effect of Calcium Chloride on the Coagulability of the Blood.*—The calcium "in vitro" test was first described by Wright<sup>15</sup> in 1893, and later advocated by Lee and Vincent<sup>1</sup> and Walters<sup>2</sup> in cases of obstructive jaundice. It consists of adding a few drops of a 1 per cent. solution of calcium chloride to a sample of blood, and recording the time it requires to clot. This is frequently found to be considerably shorter than the coagulation time of the blood without the addition of the calcium salt, according to the above inves-

TABLE III  
*Blood Serum Calcium Determinations from the Literature*

| Investigator                               | No. Cases  | Normal Calcium Values<br>Minimum and Maximum | No. Cases  | Jaundiced Calcium Values<br>Minimum and Maximum |
|--|------------|--|------------|---|
| Kirk & King <sup>8</sup> . . . . .         | 7          | 7.43 to 13.94                                | 6          | 6.94 to 11.39<br>(one as low as 4.31)           |
| Cantarow, Dodek & Gordon <sup>9</sup>      | 6          | 10.09 to 10.45                               | 10         | 9.3 to 11.3                                     |
| Snell, Greene & Rowntree <sup>10</sup> . . | ..         | .....  | 3 dogs     | 9.1 to 11.0                                     |
| Zimmerman <sup>11</sup> . . . . .          | 9 dogs     | 10.3 to 11.2                                 | 6 dogs     | 10.1 to 10.9                                    |
| Zimmerman <sup>11</sup> . . . . .          | 6 patients | 9.6 to 10.7                                  | 5 patients | 9.2 to 10.7                                     |
| Buchbinder & Kern <sup>12</sup> . . . . .  | 5 dogs     | 9.4 to 10.5                                  | 4 dogs     | 5.1 to 8.0                                      |

tigators. This fact has led to the support of the belief that there is a deficiency in the available calcium.

The above test has been carried out on many cases of obstructive jaundice in this hospital. Analysis of a series of these does not point to a deficiency in available calcium in obstructive jaundice.

The multiple-tube method for determining the coagulation time, described by Lee and White<sup>4</sup> was the one used in the following cases. Four or five tubes one centimetre in diameter are used. One cubic centimetre of blood is placed in each tube. Three drops of a 1 per cent. solution of calcium chloride are put in the last tube and in this way the calcium "in vitro" coagulation time is obtained. This is according to the original technic of Lee and Vincent.<sup>1</sup>

I have collected from the records of the Massachusetts General Hospital fifteen cases of obstructive jaundice in which this test has been carried out. In some of the cases it was repeated several times, so that in all the results of the test in twenty-three samples of blood were obtained. These figures are tabulated in Table IV. Examination of them show that in seventeen of the twenty-three tests the calcium "in vitro" time was longer than in the untreated blood, while in only six cases was it shorter. In the

latter, the decrease was practically negligible or the coagulation time of the untreated blood was within normal limits.

I believe the reason the calcium "in vitro" figures are longer than the other figures is that the tube in which the calcium is placed is usually the last tube to be tilted in order to determine the coagulation time. The important fact proven by these figures, however, is that in the great majority of these tests the addition of calcium ions did not hasten the coagulation time.

TABLE IV  
*Calcium "in vitro" Coagulation Tests in Patients with Obstructive Jaundice*

| Case | Diagnosis                     | Age and Sex | Duration of Jaundice | Degree of Jaundice | Coagulation Time in Min. | Calcium "in vitro" Coagulation Time in Min. |
|------|-------------------------------|-------------|----------------------|--------------------|--------------------------|---|
| 1    | Carcinoma of Pancreas         | 59 M        | 1 wk                 | 11* 100            | 8                        | 15  |
| 2    | Carcinoma of Pancreas         | 47 M        | 2 wks                | 11 75              | 11 1/2                   | 9   |
| 3    | Carcinoma of Pancreas         | 55 F        | 1 wk                 | 11 75              | 18                       | 27  |
| 4    | Carcinoma of Pancreas         | 61 M        | 4 wks                | 11 75              | 22                       | 18  |
| 5    | Carcinoma of Pancreas         | 57 M        | 6 wks                | 11 70              | 19                       | 16  |
| 6    | Stenosis of Common Duct       | 28 F        | 11 wks               | +++                | 12                       | 12  |
| 7    | Stenosis of Common Bile Duct  | 35 F        | 4 wks                | 11 15              | 10                       | 7   |
| 8    | Stenosis of Common Bile Duct  | 37 F        | 3 wks                | ++                 | 10                       | 12  |
| 9    | Carcinoma of Pancreas         | 60 F        | 3 wks                | 19 5               | 21                       | 22  |
| 10   | Carcinoma of Pancreas         |             |                      | 11 100 0++         | 26                       | 23  |
|      | Carcinoma of Pancreas         |             |                      |                    | 14                       | 25  |
| 11   | Stricture of Common Bile Duct | 33 F        | 5 mos                | 21 41              | 30                       | 34  |
|      | Stricture of Common Bile Duct |             |                      |                    | 14                       | 25  |
|      | Stricture of Common Bile Duct |             |                      |                    | 20                       | 23  |
|      | Stricture of Common Bile Duct |             |                      |                    | 22                       | 26  |
|      | Stricture of Common Bile Duct |             |                      |                    | 12                       | 16  |
| 12   | Carcinoma of Head of Pancreas | 48 F        | 9 wks                | 11 100+            | 10                       | 70  |
|      | Carcinoma of Head of Pancreas |             |                      |                    | 9                        | No clot in 2 hrs                            |
|      | Carcinoma of Head of Pancreas |             |                      |                    | 10                       | 7   |
| 13   | Carcinoma of Head of Pancreas | 47 M        | 3 wks                | 25                 | 16                       | 26  |
| 14   | Common Duct Stone             | 42 M        | 1 wk.                | +++                | 38                       | 33  |
| 15   | Carcinoma of Head of Pancreas | 55 M        | 4 wks                | 25 0               | 15                       | 34  |

\* I I—Icteric Index

Further proof that this test does not indicate a lack of available calcium in the blood was shown by comparing the calcium "in vitro" and sodium "in vitro" coagulation times on the blood of an animal in which obstructive jaundice had been produced by ligation and division of the common bile duct.

Blood for this purpose was obtained from animal 79, after marked jaundice had developed and the coagulation time of the blood had become greatly increased. The method used for the determination of the coagulation time was the Schwarz-Ottenberg modification of Milhan method<sup>16</sup> which is a hanging drop preparation. This was used because it requires only a small quantity of blood and it also gives a fairly definite end-point.

Determinations were made on four different occasions, over a period of six days. The blood was obtained with extreme care from the saphenous vein. A clean syringe and needle were used for each determination. Three specimens were obtained, each of 2 cubic centimetres, and all within a very few minutes of each other. No solution was added to the first specimen. In the second syringe 0.2 of a cubic centimetre of 1 per cent solution of calcium chloride, and in the third one the same amount of normal saline was

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introduced before withdrawing the blood. The latter two specimens had to be rotated gently to mix the blood and solutions. This agitation and the dilution of the blood, I think, explains why the blood samples treated with the above salts clotted more rapidly than the untreated samples.

The results are tabulated in Table V. In all instances both the calcium and the sodium "in vitro" coagulation times were shorter than the normal ones. There was notably little difference between the calcium and the sodium figures, indicating that additional calcium has no direct effect on increasing the coagulability of jaundiced blood.

TABLE V  
*Calcium and Sodium "in vitro" Coagulation Times*

| Days Post-operative | Icteric Index | Coagulation Time without Solution | Calcium Chloride Coagulation Time | Sodium Chloride Coagulation Time |
|---------------------|---------------|-----------------------------------|-----------------------------------|----------------------------------|
| 17                  | 100+          | 126 min.                          | 97 min.                           | 93 min.                          |
| 19                  | 100+          | 76 min.                           | 60 min.                           | 39 min.                          |
| 21                  | 100+          | 103 min.                          | 44 min.                           | 67 min.                          |
| 23                  | 100+          | 40 min.                           | 15 min.                           | 25 min.                          |

The effect of the intravenous administration of calcium chloride on the coagulation time was also studied in jaundiced patients who were being prepared for operation. In Table VI I have tabulated the coagulation times of nine patients with a high grade of obstructive jaundice, before and after calcium therapy. The dosage varied from 5 cubic centimetres of a 10 per cent. solution of calcium chloride to 30 cubic centimetres of a 5 per cent. solution. The number of injections varied from a minimum of two in some cases to a maximum of seven in one case.

In seven of these cases the coagulation time was found to be longer after the intravenous calcium therapy than it was before. Case 7 received seven injections without increasing the coagulability of the blood. Thus before the treatment was instituted the coagulation time was fifty-one minutes, and after the seventh injection, it was ninety-four minutes. This last figure was obtained just eight minutes after the last calcium treatment had been given, when the calcium ions in the blood should have been at a maximum. In Case 8, after six injections there was a drop from twenty-one to fourteen minutes, although after the fifth injection the coagulation time was still twenty-eight minutes. Case 9 showed a drop from thirty-eight to thirty-three minutes after two injections. Thus of these nine cases, only two showed any decrease in the coagulation time of the blood. In one of these, Case 9, the increase was negligible, and in the other, Case 8, it was questionable.

*The Administration of Calcium for Post-operative Bleeding.*—In three cases which developed post-operative bleeding, calcium chloride intravenously did not control the hæmorrhage. On two occasions it was used for a woman of thirty-seven with obstructive jaundice due to a stone in the common bile

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duct. Two operations were performed before the stone was removed, and in both instances the patient developed post-operative bleeding, which was not controlled by calcium chloride intravenously. Direct blood transfusion had to be resorted to each time. In another case of a man seventy years old with obstructive jaundice due to carcinoma of the head of the pancreas, in which a cholecystgastrostomy was done, bleeding from the wound commenced on the seventh day post-operatively. Calcium chloride given intravenously failed to check the bleeding, and it was controlled only by direct blood transfusion.

TABLE VI

*The Effect of Intravenous Calcium Chloride on the Coagulation Time in Obstructive Jaundice*

| Case | Diagnosis  | Age and Sex | Duration of Jaundice | Degree of Jaundice | No. Pre-op. Injections Calcium Chloride | Coag. Time in Minutes Prior to Injections | Coag. Time in Minutes after Injections |
|------|--|-------------|----------------------|--------------------|---|---|--|
| 1.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 46 M        | 12 mos.              | 16.0               | 3                                       | 18  | 18                                     |
| 2.   | Cholelithiasis and Carcinoma of Pancreas.....        | 39 M        | 12 days              | 21.0               | 5                                       | 32  | 33                                     |
| 3.   | Cholelithiasis with Stone in Common Bile Duct.....   | 39 F        | 2 wks.               | 16.0               | 4                                       | 18  | 30                                     |
| 4.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 75 M        | 1 wk.                | 18.75              | 2                                       | 26  | 35                                     |
| 5.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 41 M        | 2 wks.               | 18.0               | 2                                       | 26  | 30                                     |
| 6.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 45 M        | 6 wks.               | 24.0               | 2                                       | 14  | 16                                     |
| 7.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 66 M        | 11 wks.              | 19.75              | 7                                       | 41  | 94*                                    |
| 8.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 60 F        | 1 wk.                | 19.0               | 5th<br>6th                              | 21<br>21                                  | 28<br>14                               |
| 9.   | Cholelithiasis with Stricture Common Bile Duct.....  | 42 M        | 4 days               | +++                | 2                                       | 38  | 33                                     |

\* This determination was made 8 minutes after the seventh injection of calcium chloride.

The fourth occasion it was used for a woman of twenty-seven with obstructive jaundice due to a stone impacted in the common bile duct. Bleeding started following the removal of the abdominal drain on the tenth day post-operatively. The oozing again was not controllable with intravenous calcium chloride, and direct blood transfusion had to be resorted to.

It is true that in these four instances, only one injection of 5 cubic centimetres of a 10 per cent. solution of calcium chloride was used. Further delay did not seem justifiable, to determine if additional calcium treatment would be of value, so transfusion was resorted to in each case. Pre-operative preparation with intravenous calcium chloride was also used in three of the four instances cited above.

*Operative Results—Post-operative Bleeding.*—In a series of forty patients with obstructive jaundice, operated upon chiefly in the past two years at this hospital, twenty-three received pre-operative preparation with two or more injections of 5 or 10 per cent. calcium chloride, while seven-

TABLE VII  
*Post-operative Hæmorrhage in Cases of Obstructive Jaundice Prepared with Calcium Chloride Pre-operatively*

| Case | Diagnosis   | Age and Sex | Duration of Jaundice | Degree of Jaundice | No. Calcium Chloride Treatments            | Post-op. Bleeding | Operation   | Anæsthesia Duration | End-result  |
|------|---|-------------|----------------------|--------------------|--|-------------------|---|---------------------|---|
| 1.   | Cholelithiasis with Stone in Common Bile Duct.....                      | 39 F        | 2 wks.               | 16.0               | 4 Injections<br>5cc. 10 per cent.          | ++                | Cholecystectomy and Choledochostomy                     | Ether 2°            | Home  |
| 2.   | Carcinoma of Pancreas with Obstructive jaundice.....                    | 75 M        | 2 wks.               | 18.75              | 2—15cc. 5 per cent.                        | ++                | Cholecystgastrostomy                                    | Spinal 1°           | Death from hæmorrhage 15 days post-op.                  |
| 3.   | Pancreatitis with Obstructive jaundice.....                             | 41 M        | 2½ wks.              | 18.0               | 2—5cc. 10 per cent.                        | +                 | Cuolecystgastrostomy                                    | Ether 1°15°         | Home  |
| 4.   | Carcinoma of Pancreas with Obstructive jaundice.....                    | 62 M        | 6 wks.               | 24.0               | 2—5cc. 10 per cent.                        | 0                 | Cholecystgastrostomy                                    | Spinal 1°           | Death 4th day post-op.                                  |
| 5.   | Carcinoma of Pancreas with Obstructive jaundice.....                    | 46 M        | 12 mos.              | 16.0               | 3—10cc. 5 per cent.                        | 0                 | Aspiration of Gall-Bladder                              | Local               | Death 4th day post-op., broncho-pneumonia               |
| 6.   | Carcinoma of Pancreas and Cholelithiasis with Obstructive Jaundice..... | 39 M        | 12 days              | 21.0               | 5—15cc. 5 per cent.                        | +                 | Cholecystostomy and Choledochostomy                     | Spinal 2°           | Death 6th day post-op., hepatitis and broncho-pneumonia |
| 7.   | Cholelithiasis with Stone in Common Bile Duct.....                      | 42 M        | 4 days               | +++                | 2—5cc. 10 per cent.                        | 0                 | Cholecystectomy and Choledochotomy                      | Ether 2°30°         | Home  |
| 8.   | Post-op. Stricture Common Bile Duct.....                                | 33 F        | 3 mos.               | 21.0               | 3—10cc. 5 per cent.                        | 0                 | Drainage of Hepatic Duct and Transfusion                | Spinal 2°23°        | Home  |
| 9.   | Stricture Common Bile Duct with Biliary Fistula.....                    | 33 F        | 0                    | 0                  | 3—10cc. 5 per cent.                        | +++               | Transplant of Biliary Sinus in Duodenum and transfusion | Spinal 1°50°        | Home  |
| 10.  | Stone in Common Bile Duct with Jaundice and Pregnancy.....              | 27 F        | 2 wks.               | +++                | 3—5cc. 10 per cent.                        | +++               | Cholecystectomy and Choledochotomy                      | Ether 1°40°         | Home  |
| 11.  | Cancer of Pancreas with Obstructive Jaundice.....                       | 60 F        | 1 wk. +              | 19.0               | 3—10cc. 5 per cent.<br>3—30cc. 5 per cent. | 0                 | Cholecystostomy   | Spinal 30°          | Death 11th day post-op., broncho-pneumonia              |
| 12.  | Cancer of Liver with Obstructive Jaundice.....                          | 60 F        | 6 wks.               | 25.0               | 2—15cc. 5 per cent.                        | +                 | Cholecystectomy and Choledochostomy                     | Ether 2°            | Death 5th day post-op., hepatitis and pneumonia         |
| 13.  | Cancer of Biliary Passages with Jaundice.....                           | 38 M        | 8 wks.               | 31.0               | 3—10cc. 5 per cent.                        | +++               | Cholecystgastrostomy                                    | Spinal 1°44°        | Death 6th day post-op., hæmorrhage                      |

TABLE VII (Continued)

| Case | Diagnosis                                      | Age and Sex | Duration of Jaundice | Degree of Jaundice | No. Calcium Chloride Treatments                               | Post-op. Bleeding | Operation   | Anaesthesia Duration | End-result  |
|------|--|-------------|----------------------|--------------------|---|-------------------|---|----------------------|---|
| 14.  | Cancer of Biliary Passages with Jaundice       | 57 F        | 7 wks                | 18 75              | 3—10cc. 5 per cent.   | 0                 | Exploratory Laparotomy                              | Spinal 1°            | Death 15th day post-op., (?) broncho-pneumonia  |
| 15.  | Cancer of Pancreas with Jaundice               | 53 M        | 4 wks.               | 14 25              | 2—10cc. 5 per cent.   | 0                 | Cholecystgastrostomy                                | Spinal 1°            | Home  |
| 16.  | Cancer of Pancreas .                           | 66 M        | 11 wks               | 19 75              | 7—15cc. 5 per cent.   | +                 | Cholecystgastrostomy, Jejunostomy and transposition | Spinal 2°            | Death 4th day post-op., pneumonia and some hæmorrhage                                   |
| 17.  | Stricture Common Bile Duct with Jaundice . . . | 36 F        | 3 mos.               | ++ ++              | 3—10cc 5 per cent. +  | ++ +              | Plastic Operation to Common Bile Duct               | Ether 1°50'          | Death 2nd day post-op., hæmorrhage  |
| 18.  | Stricture Common Bile Duct with Jaundice . . . | 37 F        | 12 mos.              | ++ +               | 3—10cc. 5 per cent.   | +                 | Anastomosis of Hepatic and Common Duct              | Ether 2°30'          | Death 9th day post-op.  |
| 19.  | Cancer of Head of Pancreas                     | 47 M        | 2 wks.               | 11 50 +            | 2—10cc 5 per cent.  | 0                 | Cholelithoduodenostomy                              | Ether 2°15'          | Home  |
| 20.  | Cancer of Pancreas .                           | 47 M        | 4 wks                | 11 70              | 3—10cc. 5 per cent.   | ++ +              | Cholecystgastrostomy                                | Ether 1°15'          | Death 2nd day post-op.  |
| 21.  | Stricture Common Bile Duct                     | 47 M        | 2 wks.               | 11 50 +            | 3—10cc. 5 per cent  | ++ +              | Cholelithotomy                                      | Ether 1°30'          | Home  |
| 22.  | Cancer of Pancreas .                           | 59 M        | 4 wks                | 11 100             | 3—10cc. 5 per cent.   | ++                | Cholecystgastrostomy                                | Ethylene 1°25'       | Home  |
| 23   | Toxic Hepatitis .                              | 30 M        | 3 wks.               | 15 0               | 3—10cc. 5 per cent. Ca. Gluconate gms. xx for 19 days pre-op. | +                 | Exploratory Laparotomy                              | Spinal 30'           | Home against advice; still bleeding 19th day post-op. Received 2 post-op. transfusions. |

TABLE VIII

*Post-operative Hemorrhage in Cases of Obstructive Jaundice Not Prepared with Calcium Chloride Pre-operatively*

| Case | Diagnosis  | Age and Sex | Duration of Jaundice | Degree of Jaundice | No. Calcium Chloride Treatments | Post-op. Bleeding | Operation  | Anesthetic Duration | End-result   |
|------|--|-------------|----------------------|--------------------|---------------------------------|-------------------|--|---------------------|--|
| 1.   | Carcinoma of Pancreas with Obstructive Jaundice..... | 50 M        | wks.                 | 16.0               | 0                               | 0                 | Cholecystostomy  | Ether 1°10'         | Death in 36 hrs.                                       |
| 2.   | Cholelithiasis with Stone in Common Bile Duct.....   | 37 M        | 2 wks.               | 7.0                | 0                               | 0                 | Cholecystectomy and Choledochostomy                          | Ether 2°            | Home   |
| 3.   | Cholelithiasis with Jaundice                         | 45 M        | 4 days               | 15.0               | 0                               | 0                 | Choledochostomy  | Ether 2°            | Home   |
| 4.   | Cholelithiasis with Stone in Common Bile Duct.....   | 48 F        | 10 wks.              | 5.25               | 0                               | 0                 | Cholecystectomy and Choledochostomy                          | Ether 1°10'         | Home   |
| 5.   | Carcinoma of Pancreas with Jaundice.....             | 44 M        | 6 wks.               | 10.13              | 0                               | 0                 | Cholecystgastrostomy   | Ether 1°            | Home   |
| 6.   | Cholelithiasis, Acute Yellow Atrophy.....            | 50 F        | 5 days               | 12.0               | 0                               | 0                 | Cholecystectomy and Choledochotomy                           | Ether 2°            | Death 50th day post-op., acute yellow atrophy          |
| 7.   | Carcinoma of Pancreas with Jaundice.....             | 47 M        | 3 wks.               | 25.0               | 0                               | 0                 | Exploratory Laparotomy                                       | Spinal 1°           | Death  |
| 8.   | Infectious Hepatitis.....                            | 51 M        | 7 wks.               | 24.75              | 0                               | +                 | Exploratory Laparotomy                                       | Ether 45'           | Home   |
| 9.   | Cholelithiasis with Stone in Common Bile Duct.....   | 49 F        | 4 wks.               | 13.0               | 0                               | ++                | Cholecystectomy and Choledochotomy                           | Ether               | Home   |
| 10.  | Same.....  | 50 F        | 5 wks.               | 17.25              | 0                               | ++                | Choledochostomy  | Spinal 1°30'        | Home   |
| 11.  | Stone in Common Bile Duct with Biliary Fistula.....  | 39 F        | 0                    | 0                  | 0                               | +                 | Choledochostomy  | Ether 2°30'         | Home   |
| 12.  | Carcinoma of Pancreas with Obstructive Jaundice..... | 59 M        | 1 wk.                | 21.3 mg.           | 0                               | 0                 | Cholecystgastrostomy   | Spinal 1°20'        | Home   |
| 13.  | Stricture Common Bile Duct.....                      | 28 F        | 11 wks.              | ++                 | 0                               | 0                 | Choledochoduodenostomy                                       | Ether 2°30'         | Home   |
| 14.  | Stricture Common Bile Duct.....                      | 37 F        | 4 wks.               | ++                 | 0                               | 0                 | End-to-end Suture Common Bile Duct                           | Ether 2°20'         | Home   |
| 15.  | Cholelithiasis with Jaundice.....                    | 48 F        | 1 wk.                | 20.81              | 0                               | 0                 | Cholecystectomy and Choledochotomy and Transfusion for Shock | Ether 1°30'         | Home   |
| 16.  | Cholelithiasis with Jaundice.....                    | 71 M        | 2 wks.               | 11.42              | 0                               | 0                 | Cholecystectomy and Choledochotomy                           | Ether 1°45'         | Death 20th day post-op., pneumonia and cardiac failure |
| 17.  | Carcinoma of Pancreas with Jaundice.....             | 49 M        | 2 wks.               | 11.70              | 0                               | 0                 | Cholecystgastrostomy   | Ether 1°15'         | Home   |



teen did not receive any calcium chloride. (See Tables VII and VIII.) Bleeding took place in fifteen cases, or 65 per cent. of the former group. This varied in severity from strongly positive guaiac tests in the stools to death from uncontrollable hæmorrhage. The most striking example was Case 16 who died four days post-operatively from broncho-pneumonia and hæmorrhage. This patient received in all seven injections of 15 cubic centimetres of a 5 per cent. solution of calcium chloride. A transfusion was also given the day of operation, but despite this and the intensive calcium therapy, bleeding took place, which definitely hastened his death.

In the group operated upon without calcium therapy, bleeding took place in only four cases, or 23 per cent. of the seventeen. The two groups are similar in that the degree and duration of the jaundice was marked in practically all cases. Then also, the extent of the operations on the biliary system in the two groups was nearly the same. The remainder of the pre-operative preparation was similar in both groups. The anæsthetic used in most of these cases was ether, although spinal was used in some cases of both groups. Local anæsthesia and ethylene were used in one case each.

According to these figures, the cases which received no calcium chloride did not have such a high percentage of post-operative hæmorrhage as the ones which were prepared pre-operatively with it. The reason for this is partly due to the fact that seven of these seventeen cases were selected cases, as they had slow blood sedimentation rates. According to a recent article by the author<sup>17</sup> it can be predicted that post-operative hæmorrhage is not likely to occur as long as the sedimentation rate remains slow. On the other hand it is unlikely that calcium chloride injections increase the hæmorrhagic tendency, as the above figures seem to indicate. The most important conclusion to be drawn, however, is that calcium chloride does not seem to guard against post-operative hæmorrhage.

*The Effect of Calcium Chloride Therapy on the Blood Sedimentation Rate.*—The sedimentation rate of the blood seems to be of value in predicting which patient may bleed post-operatively.<sup>17</sup> Patients with a slow or normal rate do not bleed, while those with rapid rates are apt to bleed. Calcium chloride therapy had no effect on the sedimentation rate in five cases on which the test was done before and after the treatment. The results are tabulated in Table IX. Four of these cases had very rapid rates and in all the sedimentation rate was more rapid following the calcium therapy. This was undoubtedly because the patients were becoming worse between the two determinations. In the fifth case, the rate was relatively slow before, and remained essentially the same following the treatments.

*The Effect of Calcium Chloride Therapy on the Post-operative Mortality Rate.*—The recent investigations of Lamson, Minot and Robbins,<sup>18</sup> in reference to the protective action of calcium in cases of carbon tetrachloride intoxication, is perhaps evidence that calcium may be of value in cases of obstructive jaundice with severe liver damage. Study of the causes of death in the above series of forty cases does not point to a protective action from

# ANTI-HÆMORRHAGIC USE OF CALCIUM

TABLE IX

*Effect of Calcium Chloride on the Sedimentation Rate of the Blood*

| Case | Diagnosis                    | Age and Sex | Duration | Degree | No. Calcium Chloride Injections                          | Sed. Rate Before | Sed. Rate After |
|------|------------------------------|-------------|----------|--------|--|------------------|-----------------|
| 1.   | Toxic Hepatitis.....         | 36 M        | 3 wks.   | 15.0   | 3—10cc. 5 per cent. and Ca. gluconate Gr. xx for 18 days | 9 mm.            | 11 mm.          |
| 2.   | Carcinoma of Bile Ducts..... | 48 F        | 6 wks.   | 30.0   | 3—10cc. 5 per cent.                                      | 65 mm.           | 74 mm.          |
| 3.   | Carcinoma of Pancreas.....   | 38 M        | 8 wks.   | 31.0   | 3—10cc. 5 per cent.                                      | 32 mm.           | 40 mm.          |
| 4.   | Carcinoma of Pancreas.....   | 53 M        | 4 wks.   | 19.75  | 7—15cc. 5 per cent.                                      | 48 mm.           | 50 mm.          |
| 5.   | Carcinoma of Bile Ducts..... | 57 F        | 7 wks.   | 18.75  | 3—10cc. 5 per cent.                                      | 48 mm.           | 58 mm.          |

the pre-operative use of intravenous calcium chloride. In the group of twenty-three patients treated with calcium chloride there were thirteen deaths, a post-operative mortality rate of 56.5 per cent. Nine of these were due directly to hæmorrhage or hepatic insufficiency, a mortality rate of 39.1 per cent.

In the group of seventeen patients who received no calcium therapy, there were three deaths, a mortality rate of 17.6 per cent. None of these was due to hæmorrhage. Two of these deaths were directly related to hepatic insufficiency, a mortality rate of only 11.7 per cent. from this cause. (See Tables VII and VIII.)

*Discussion.*—The cause of the lowered coagulability of the blood in cases of obstructive jaundice has been considered to be due to the presence of bile pigments in the circulation. The mechanism by which these pigments delay the coagulation of the blood has never been fully explained. A number of years ago the theory was advanced that the bile pigments united with the available calcium in the blood-stream, and this in some way changed the calcium into a non-utilizable form for the process of coagulation.

This theory has never been satisfactorily proven, but it has been accepted by many as the most logical explanation of the lowered coagulability of the blood in obstructive jaundice. Furthermore, the pre-operative preparation with intravenous injections of a soluble calcium salt in cases of obstructive jaundice has been based on this assumption.

Zimmerman<sup>11</sup> in 1927 challenged the efficacy of calcium therapy in these cases. He pointed out that there is no sound theoretical basis for its possible effect on the coagulability of the blood.

The tendency to bleed does not depend on the degree nor the duration of the jaundice. Some cases of biliary fistula with no retention of bile pigments in the blood-stream have a very marked bleeding tendency. For such cases the above theory will not suffice.

Quantitative determinations of the serum calcium, both in experimental and clinical obstructive jaundice, have shown no deficiency nor accumulation. The addition of calcium chloride to jaundice blood "in vitro" in the majority of cases reported here does not increase the coagulability of the

blood. Experimentally in one case the addition of sodium chloride "in vitro" produced a shortening of the coagulation time equal to that by the addition of calcium chloride. This shortening of the coagulation time was probably due to agitation and dilution of the specimens, and not due to any specific effect of the sodium or calcium ions.

After the administration of calcium chloride intravenously to patients with obstructive jaundice, the coagulability of the blood was not increased in the majority of cases. The incidence of post-operative hæmorrhage was not decreased in a series of patients which received calcium therapy pre-operatively, as compared with a similar group which did not receive calcium. The administration of calcium chloride intravenously does not stop post-operative hæmorrhage at the time it is taking place. In the above group of cases prepared with intravenous calcium chloride the mortality rate from hæmorrhage and hepatic insufficiency was higher than in the group which received no calcium therapy.

If a case of obstructive jaundice presents a rapid blood sedimentation rate, indicating a hæmorrhagic tendency, a direct blood transfusion, given within twenty-four hours of operation, and repeated if necessary, is the most valuable and effective means of protecting against post-operative bleeding that we have at the present time.

#### CONCLUSIONS

1. The administration of calcium in obstructive jaundice has no theoretical or practical basis for the prevention of post-operative hæmorrhage.

2. The lowered coagulability of the blood in cases of obstructive jaundice does not seem to be due to a deficiency nor an abnormality of the blood calcium.

3. The most effective means of preventing and stopping post-operative hæmorrhage in obstructive jaundice at present is repeated direct blood transfusions used in conjunction with a high pre- and post-operative carbohydrate and fluid intake.

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# THE USE OF EXPLORING NEEDLES AND SHADOW-CASTING MEDIA IN THE DIAGNOSIS OF HEPATIC AND PERIHEPATIC ABSCESS

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THE use of satisfactory shadow-casting media for observing the contour of hollow viscera or the shape and extent of cavities has become of salient importance to the medical man of today. The use of opaque substances in abdominal viscera has largely eliminated the necessity for exploratory operations.

In hepatic or perihepatic abscess, however, it still seems to be the opinion of many that usually the diagnosis can be made only by an exploratory operation. The diagnosis is often very difficult in hepatic and perihepatic abscess. The history is in most cases suggestive. Previous intra-abdominal pathology may suggest the possibility, but in obscure abdominal cases where symptoms of infection are present, it is well to bear in mind that there may be an abscess of the liver or perihepatic spaces. Irregular temperature, sweating, wasting, and progressive secondary anæmia should arouse suspicion, and if added to this the patient complains of some fullness, discomfort or pain in the upper abdomen, the condition warrants further examination.

The X-ray is frequently of extreme value in suggesting the location of a suppurative process about the liver. The elevation and the diminished mobility of the diaphragm, and in some instances an alteration of the contour resulting from a local collection of pus beneath the diaphragm, may point very decidedly to the spot to which the exploring needle should be directed.

The active treatment of hepatic or perihepatic abscess is necessarily surgical and it should be instigated as soon as practical after the diagnosis is made. This is a condition in which time is an important factor, therefore early recognition with proper treatment should lower the very high fatality rate which now exists. If the history of onset and course are correlated with a carefully made X-ray examination, and is then followed by localization with the exploring needle, injection of iodized oil and further X-ray pictures, there may be prevented the frequent procrastination in the application of proper surgical measures.

Both hepatic and perihepatic abscesses, whether occurring from amœbic infection or resulting from pyogenic organisms, will be considered together in the question of early diagnosis by the use of the exploring needle and injection of iodized oil.

One is rather hesitant in advocating the exploring needle after reading in the surgical literature such statements as, "Aspiration has been recom-

## DIAGNOSIS OF HEPATIC ABSCESS

mended by some. It is unsurgical"; and "For years it has been common practice to employ the aspirating needle in making a diagnosis. I am glad the practice is going out of fashion. I cannot lay sufficient emphasis on the futility of this custom." And yet those of us who have "done time" in the Tropics, where pathological conditions of the liver region are so common as compared to the frequency in the United States, cannot but feel that the exploring needle has a very definite place in suspected hepatic or perihepatic abscess. We are somewhat inclined to agree with Sir Leonard Rogers when he states, in speaking of amoebic abscess, "There is probably no serious tropical disease in which so much advance has been made during the last

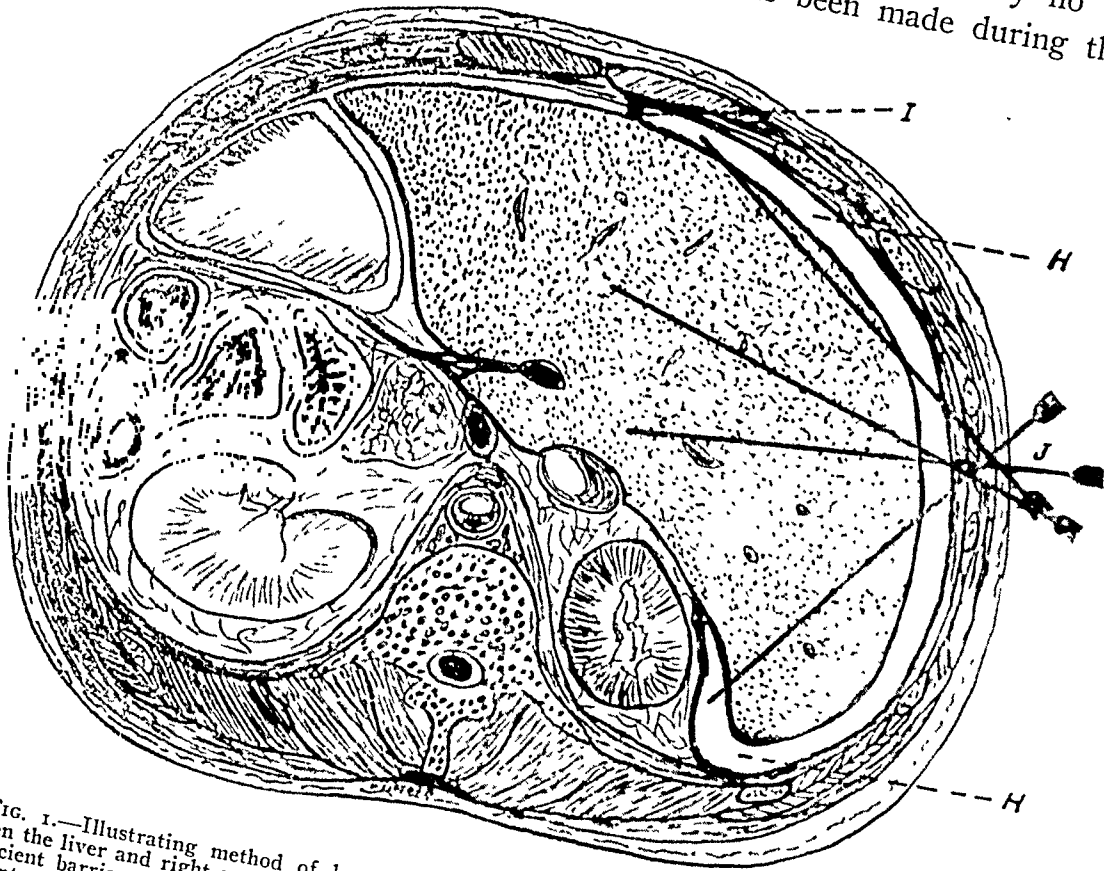


FIG. 1.—Illustrating method of locating hepatic or perihepatic abscesses. *I*.—Suspensory (falciform) ligament of the liver, which forms an efficient barrier to abscesses anterior to the liver. *J*.—Point of insertion of needles in ninth or tenth interspace in exploring for hepatic or perihepatic abscess. *H*.—Potential cavity between the liver and right costal area. Cross-section at level of first lumbar vertebra.

quarter of a century, both in prevention and cure, as in amoebic hepatitis and its sequel, liver abscess. . . . Aspiration is the method of choice." Sir Frank Powell Conner states, "It must be explained at the onset that the treatment of amoebic liver abscess by open incision is becoming an increasing rare operation. It is not a question of timid surgery."

The patient with a hepatic or perihepatic abscess is usually acutely ill. The condition of the patient becomes progressively worse unless the abscess is diagnosed and treated early. The use of the exploring needle as a diagnostic means permits of an early diagnosis without resorting to a major

operation, and with a minimum of shock. For those abscesses resulting from amoebic infection which are found to be sterile (and this includes, statistics show, 86 per cent. of all amoebic abscesses), the aspirating needle is not only of importance for diagnosis but also for treatment. In hepatic and perihepatic abscesses resulting from pyogenic organisms or in which pyogenic organisms are present in smear or culture, the aspirating needle is recommended only as a means for diagnosis and not as a means of treatment.

The exploring needle has its limitations as it can be used with safety only in hepatic or perihepatic abscess involving the right lobe of the liver. However, when one considers that more than 80 per cent. of amoebic

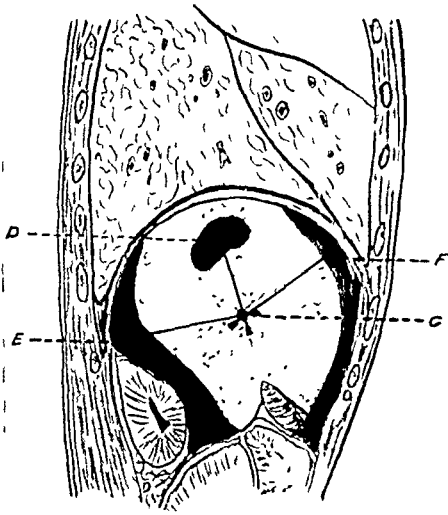


FIG. 2.—Diagram taken to the right of the mid-line. *D*.—Liver abscess. *E*.—Abscess posterior perihepatic space. *F*.—Abscess anterior perihepatic space. *G*.—Point of insertion of needles for diagnosis and localization of hepatic or perihepatic abscess ninth or tenth intercostal space.

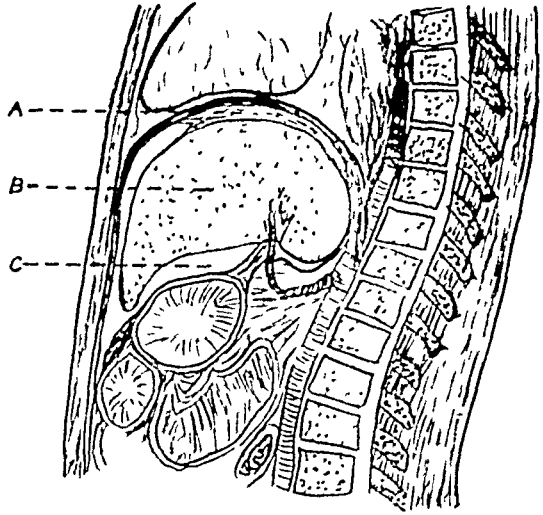


FIG. 3.—Diagram illustrating potential perihepatic spaces. *A*.—Extra peritoneal space corresponding to the fore spot of the liver. *B*.—The liver. *C*.—Potential cavity about liver where abscess may occur.

abscesses occur in the right lobe, and that seldom is a perihepatic abscess found except about the right lobe, its range of usefulness is great.

In considering exploration for an abscess cavity, it is well to remember that on the right side there are three perihepatic spaces where abscess may be found. The anterior perihepatic space lies between the superior, anterior and to some extent the lateral aspect of the right lobe of the liver and below the diaphragm. Its left border is the falciform ligament, and its right may be at a level with the right lateral ligament. The space is usually limited below in case of suppuration by adhesions between the greater omentum, the transverse colon or between the liver and the abdominal or chest wall.

The second space of importance is the posterior perihepatic space. It lies beneath the right lobe of the liver. Above and posteriorly lies the diaphragm and separated only by the parietal peritoneum is the right kidney.

The right lateral ligament of the liver somewhat limits it from above. Below the transverse colon by adhesions usually forms the lower boundary.

The right extraperitoneal space is a potential cavity formed of loose fibrous tissue, corresponding to the bare area of the liver. It is bounded by the liver on the one side and by the fibrous and muscular tissue of the diaphragm on the other. It is limited laterally by the lateral ligament of the right lobe of the liver and above and below by the coronary ligament and reflected peritoneum. The formation of an abscess in this space may result from extension from a liver abscess, by extension from an anterior or a posterior perihepatic abscess, or following suppuration of the abdominal cavity by extension *via* the lymphatics, or from purulent infections above the diaphragm.

With the patient lying on his back, or with the right side elevated above the left, on the operating or fluoroscopic table, the liver dullness is carefully mapped out. If there are no signs of a pointing abscess, and there will not be unless unnecessary delay in attempting diagnosis has occurred, the point at which the exploring needle is to be inserted is determined upon and the area infiltrated with novocaine. If the X-ray and physical examination indicate obliteration of the costophrenic angle, it is quite safe to use the ninth interspace in the anterior or mid-axillary line. If the X-ray shows no obliteration of the costophrenic angle, it is safer to use the tenth interspace.

The regular spinal puncture needle with fairly blunt point with a three-and one-half-inch reach is the safest type of needle. For the posterior or anterior perihepatic spaces, however, a longer needle with at least a four-inch reach may be required.

Insert the needle slowly after penetrating the chest wall. If slight resistance is encountered and the general direction of the needle gives assurance that one is not against the capsule of the liver or a large vessel, withdraw the needle slightly and alter its course to one side. The advantage of the spinal puncture needle or other blunt-pointed needle is that one cannot penetrate important structures without having first encountered a feeling of resistance greater than that given by liver tissue itself. Likewise, when attempting to locate an abscess of the perihepatic spaces, the needle is inserted in the chest wall. If pus is present between the chest wall and the liver, pus will be encountered before the needle enters the liver. If no pus is encountered, direct the needle in the direction of the anterior or the posterior perihepatic space. This will require going through liver tissue. If no abscess is encountered in liver tissue, when the capsule is reached slight resistance will be felt. Being sure that no important structures can be at the point of the needle by carefully estimating the distance and direction of the needle, penetrate the capsule. The feeling of resistance against the needle is followed by a feeling of non-resistance as the needle enters the abscess cavity. This is very similar to that experienced in doing a spinal puncture as the needle penetrates the membranes and enters the spinal canal.



Aspirate thirty to sixty cubic centimetres of pus, depending upon the ease of aspiration, and inject the iodized oil. A smaller quantity of fluid should be injected than was withdrawn. It is necessary to know whether the iodized oil will sink or float upon the surface of the purulent fluid. The iodized oil used in the illustrations is heavier than water and the usual abscess fluid and will not mix with it but will sink to the lowest level.

The patient may now be placed under the fluoroscope or pictures may be taken for permanent record, with the patient turned so that the boundaries of the cavity will be determined as the iodized oil changes its position to reach the lowest level.

During this time the aspirated pus is being examined for pyogenic organisms. The character of the pus may clearly indicate that it is an amœbic



FIG. 4.—Abscess of the liver. After aspiration of three ounces of pus, one ounce of iodized oil was injected through needle. This very definitely determines its size, shape and boundaries.



FIG. 5.—Lateral view showing abscess with one ounce of iodized oil injected into the cavity. Its position in relation to the sternum and vertebra is definitely outlined. The shadow has an hour glass constriction. *D.* It is probable that the liver abscess has secondarily invaded the extra-peritoneal perihepatic space. This was an amœbic abscess.

abscess or that it is the result of a decidedly pyogenic infection. It is important to know, however, in case it appears to be an amœbic abscess, whether the amœbic pus has been secondarily infected. If it has been then incision and drainage will probably be required. If it is a sterile amœbic abscess as more than 80 per cent. will be, no further operative measures will be required beyond the continued aspiration of all pus available. However, at a later date one or more subsequent aspirations may be necessary. It is therefore desirable that one definitely localize the abscess and determine its size and shape as an aid to future aspirations. It is sometimes difficult to again locate a small liver abscess for aspiration although one may feel he knows quite well its general direction as revealed by a former aspiration. However, if the abscess cavity is injected with iodized oil at the first aspira-

tion and X-rays are made in two planes, the cavity is definitely localized in its relation with other anatomical structures.

In exploring the liver or perihepatic spaces it is easier if three or more needles are used. The first needle being inserted and no abscess encountered, it is left in position. When the second needle is inserted and no abscess found, it also is left in place. By leaving the needles in place the direction and area explored are definitely known and it is much easier with the third needle to explore remaining areas of the right lobe.

Having located the abscess and by means of iodized oil definitely determined its boundaries, and having made smears to determine the presence of pyogenic organisms, effective treatment can now be rendered the patient. Should it be found to be an amœbic abscess, sterile as regards pyogenic organisms, aspiration of the abscess one or more times with intramuscular injections of emetine hydrochloride will probably be all that is required. Open drainage in case of sterile amœbic abscess is no more to be recommended than it is in tuberculous abscesses elsewhere. In each case secondary infection will almost certainly occur and prolonged suppuration will result.

If pyogenic organisms are present in smear or culture, incision and drainage offers the greatest hope. This should, as a rule, be done at once although in acutely ill patients aspiration of the cavity at the time of exploration may put the patient in better condition for a second stage a day later. However, delay in draining a suppurative process cannot be advised except in rare cases.

In searching the literature one is impressed by the fact that various prominent surgeons seem to be convinced that one single method of approach is superior to others. Some advise the abdominal route for all abscesses irrespective of their location, as the desirable one. Others feel that the lateral approach through the intercostal spaces is the only proper method. Even in the intercostal route some advise only going by the supraphrenic route rather than below the diaphragm, while others remain below the diaphragm entirely.

The efficient method of approach can be determined by a definite localization of the abscess and the route used which is the shortest, the least traumatizing to important structures and therefore the least shocking, and which will insure satisfactory drainage.

It would seem absurd to suggest that an abscess at the points D or E in Fig. 2 could be drained with the least trauma or that satisfactory drainage could be established through an abdominal incision. Neither would a posterior or even a low intercostal incision be satisfactory for draining an abscess at point F in Fig. 2, when it is evident that it is easily accessible through a small incision in the anterior abdominal wall.

It is true there may be only one satisfactory route of approach and that route can best be determined in the great majority of cases by definite visualization of the abscess cavity by means of some opaque substances such

as iodized oil and choosing the route which is the shortest, which establishes satisfactory drainage and which is least shocking to a seriously ill patient.

By careful localization of the abscess instead of an exploratory operation the 50 per cent. mortality rate now attributed to perihepatic abscesses should be materially lowered.

It may be that the exploring needle is an "unsurgical procedure" although I do not think so. But if it is, does it not seem better to have a live patient

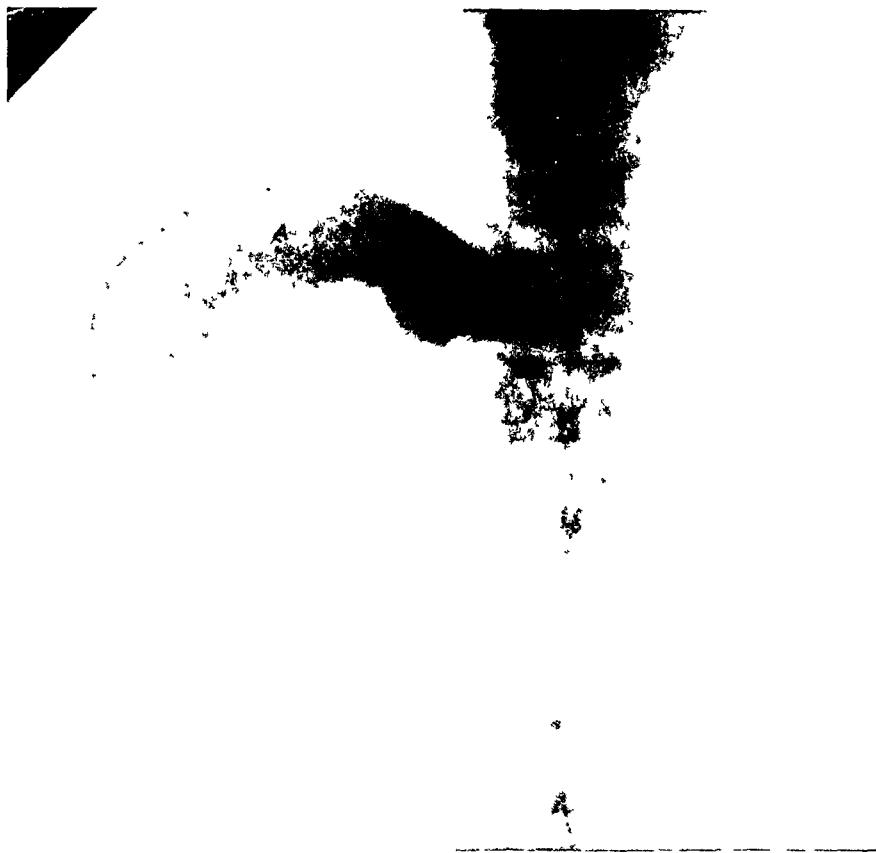


FIG. 6—Patient with perihepatic abscess. The exploring needle was inserted in the ninth interspace anterior axillary line. Pus was found in the anterior perihepatic space. Thirty cubic centimetres of pus withdrawn and twenty cubic centimetres of iodized oil injected through needle. The oil at once sank to the lowest level below the diaphragm (*A*). Patient lying flat on his back.

diagnosed or treated by the aspirating needle rather than a seriously shocked or dying patient who has received the benefit of a thoroughly surgical procedure?

#### SUMMARY

The exploring needle has a definite place in the diagnosis of hepatic and perihepatic abscess, and when used for injection of iodized oil the definite location, size and shape of the abscess can be determined. The site of the abscess is not entirely sufficient datum for successful treatment but the extent of the cavity in all directions is important.

## DIAGNOSIS OF HEPATIC ABSCESS

The aspirating needle cannot be used with safety in the left lobe of the liver or left perihepatic spaces.

The exploring needle can be used without a general anæsthetic. In the acutely ill patient the procedure gives no appreciable shock and the subsequent incision and drainage, if indicated, can be by the route that is shortest and least shocking.

The spinal puncture needle or similar blunt needle adds to the safety of the procedure.

The aspirating needle is of value both in diagnosis and in treatment of amœbic abscesses of the liver or of those that have extended into the perihepatic spaces, provided secondary infection has not occurred. The presence of pyogenic organisms is an indication for incision and drainage.

There is usually only one satisfactory route of approach to an hepatic or perihepatic abscess and that route can be determined in the majority of cases by the definite localization of the boundaries of the cavity after injection of some opaque substance.

# AN INVESTIGATION OF THE FUNCTIONS AND SYMPTOMS OF THE SURGICALLY DRAINED GALL-BLADDER\*

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ONE rarely hears the contention today that cholecystostomy is the operation of choice in the surgical treatment of gall-bladder disease. It is common knowledge, however, verified by statistics from leading hospitals and surgical clinics, that this operation is still being performed. A certain number of these patients find their way back to the surgeon for unrelieved or recurrent symptoms, or for symptoms in which an estimation of the remaining gall-bladder as a total or contributing factor is highly desirable.

With these facts in mind, a number of patients who had cholecystostomy previously performed were recalled to the Jefferson Hospital for examination and study. Five of these had had their primary operation elsewhere. Their course since operation and present physical condition was determined and cholecystograms were made. The data presented were collected from thirty-six such patients and have been arranged under separate headings and presented in table form.

It was felt that the patients treated for empyema and common duct stones were of sufficient importance to warrant more detailed reports. These are shown, therefore, as distinct sub-groups.

Information on the patients that came to subsequent operations is likewise given in more detail.

Patients indicated as "Improved" in the table showing clinical results have all complained, at some time since operation, of belching and epigastric fullness of varying degree. Nine in this group have had one or more attacks of colic.

Cholecystography was chosen as the best available method of measuring gall-bladder functional capacity. One must bear in mind, as pointed out by its originator,<sup>6</sup> that four essential steps are necessary before a shadow of the gall-bladder can be obtained by X-ray after the administration of an opaque substance. They are: (1) access to the liver for the substance; (2) its secretion into the bile; (3) access to the gall-bladder by the patency of the cystic duct; (4) sufficient concentration within the gall-bladder.

The oral administration of tetraiodophthalophenon was used in this investigation. It is known that vomiting and diarrhoea by diminishing absorption can introduce an error.<sup>6</sup> All patients exhibiting these to any appreciable degree were discarded. Since discernible liver disease may interfere with secretion of the dye into the bile, one such patient was likewise discarded.

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\* Read before the Philadelphia Academy of Surgery, May 5, 1930.

## THE SURGICALLY DRAINED GALL-BLADDER

Excluding obvious liver disease the percentage of error in cholecystography by method used from failure of secretion of bile has been shown to be less than 1 per cent.<sup>6</sup>

### LESIONS FOUND AT OPERATION

|  | Number | Per Cent. |
|--|--------|-----------|
| Chronic cholecystitis<br>Gall-bladder stones                             | 32     | 88.8      |
| * Empyema (gangrene)   | 7      | 19.4      |
| * { Chronic cholecystitis<br>Common duct stones<br>Gall-bladder stones } | 6      | 16.6      |
| Chronic cholecystitis without stones                                     | 4      | 11.1      |

### CLINICAL RESULTS

|              | Number | Per Cent. |
|--------------|--------|-----------|
| Symptom-free | 18     | 50        |
| Improved     | 14     | 38.8      |
| Unimproved   | 4      | 11.1      |

From all the splendid experimental work done on the gall-bladder its normal functions have been determined to be: (1) the storage of bile; (2)

|              | Gall-bladder<br>Visualized | Gall-bladder<br>Not Visualized |        |           |              | Normal<br>Response |           |
|--------------|----------------------------|--------------------------------|--------|-----------|--------------|--------------------|-----------|
|              | Number                     | Per Cent.                      | Number | Per Cent. | Total Number | Number             | Per Cent. |
| Symptom-free | 4                          | 11.1                           | 14     | 38.8      | 18           |                    |           |
| Improved     | 2                          | 5.5                            | 12     | 33.3      | 14           | 1                  | 2.7       |
| Unimproved   | 1                          | 2.7                            | 3      | 8.3       | 4            |                    |           |
| Totals       | 7                          | 19.4                           | 29     | 80.5      | 36           |                    |           |

the concentration of bile; (3) its expulsion on demand into the duodenum.  
<sup>4, 1, 2, 3, 5</sup> The concentration is brought about by the mucosa through the absorption of water.<sup>4</sup> Since the production of a cholecystogram clearly depends upon the concentration of an opaque dye in the gall-bladder,<sup>6</sup> one

\* Included in first group of chronic cholecystitis and gall-bladder stones.

would expect, therefore, to find the mucous membrane an essential factor for this concentration. That this is true has been shown experimentally.<sup>7</sup>

The expulsion or out-flow of bile into the duodenum is due to the contraction of the smooth muscle within its walls.<sup>1</sup> This contraction may be brought about by the ingestion of fats, and also by other means not pertinent to this discussion.

Of the entire group comprising thirty-six patients, there are twenty-seven females and nine males. The average time since operation is forty-six

## EMPHYEMA OF GALL-BLADDER

| Case  | Time Since Operation in Months | Symptoms   | Subsequent Operations             | Findings at Subsequent Operations  | Cholecystogram                 |
|-------|--------------------------------|--|-----------------------------------|--|--------------------------------|
| E. D. | 40                             | Two mild attacks of pain                                 | Refused operation                 | .....  | "Gall-bladder not visualized." |
| E. M. | 6                              | Pain, jaundice, fistula                                  | Cholecystectomy, excision fistula | Chronic cholecystitis with empyema and gall-bladder stones, common duct stones | "Gall-bladder not visualized." |
| E. A. | 38                             | Pain, gall-bladder fistula                               | Cholecystectomy, excision fistula | Chronic cholecystitis with empyema, cystic duct stone                          | "Gall-bladder not visualized." |
| H. F. | 6                              | Symptom-free   | None                              | .....  | "Gall-bladder not visualized." |
| J. S. | 36                             | Symptom-free   | None                              | .....  | "Gall-bladder not visualized." |
| E. S. | 24                             | Epigastric fullness, belching                            | None                              | .....  | "Gall-bladder not visualized." |
| M. G. | 63                             | Indigestion, dizziness, Blood-pressure, $\frac{180}{90}$ | None                              | .....  | "Gall-bladder not visualized." |

months. The longest period is 230 months and the shortest six months. The average morbidity period is twelve weeks.

All of the patients of empyema and the cases having common duct stones also had gall-bladder stones. From the empyema group two patients had subsequent cholecystectomies and one of these two had common duct stones as well. If the latter be excluded, it will be seen that none of the common duct cases, as such, came to subsequent operation. Only two patients in the empyema group are symptom-free: one thirty-six and the other six months after operation. Three of the common duct patients are symptom-free without secondary operation.

As pointed out previously, one known function of the gall-bladder is the

## THE SURGICALLY DRAINED GALL-BLADDER

ability of its mucous membrane to absorb water and thereby concentrate its contents.<sup>4</sup> The cholecystograms from the patients presented indicate that this function is entirely lost in 80 per cent. and impaired in 17.3 per cent. of the remaining 20 per cent. Only one, or 2.7 per cent., indicated normal function. This indicates very clearly that the function of concentration is severely impaired or completely lost in the surgically drained gall-bladder.

Obviously a gall-bladder must be visualized on a cholecystogram before any indication of its capacity or ability to empty can be obtained. It has been shown that severe injury to the gall-bladder resulting in fibrosis markedly inhibits its emptying time.<sup>3</sup> Of the seven gall-bladders visualized in this series, five showed impaired contraction. These represent, however, only 13 per cent. of the entire group, making these findings of relatively little value.

COMMON DUCT STONES

| Case   | Time Since Operation in Months | Symptoms   | Cholecystograms                | Subsequent Operations |
|--------|--------------------------------|--|--------------------------------|-----------------------|
| F. N.  | 9                              | Symptom-free   | "Gall-bladder not visualized." | None                  |
| A. C.  | 41                             | Several attacks of colic with jaundice, symptom-free twelve months | "Gall-bladder not visualized." | None                  |
| A. G.  | 25                             | Two attacks of colic, symptom-free fifteen months                  | "Gall-bladder not visualized." | None                  |
| L. H.  | 62                             | No pain, occasional indigestion                                    | "Gall-bladder not visualized." | None                  |
| A. S.  | 41                             | Symptom-free   | "Gall-bladder not visualized." | None                  |
| E. M.* |                                |  |                                | Cholecystectomy       |

\* See E. M. under Empyema of Gall-bladder

The size of the gall-bladders visualized on the cholecystograms is entirely within normal limits, which would indicate no appreciable loss in capacity in 19.4 per cent. of the patients. In all of the five patients that came to subsequent operation, however, the gall-bladders were shrunk and their volume capacity very definitely diminished, but these gall-bladders were not visualized on the cholecystogram. This may be explained by a difference in the degree of fibrosis of the gall-bladder walls, though we do not have sufficient evidence to substantiate such a claim.

Eighteen, or 50 per cent., of those studied have remained symptom-free. All of these gave cholecystograms indicating absent or impaired function. Clearly, these findings indicate little if any relation between function and symptoms in the externally drained gall-bladder.

The patients having subsequent cholecystectomies all had gall-bladder stones at the primary operation. There is absolute knowledge that in two of these cases all stones were not removed at this operation.



SUBSEQUENT ABDOMINAL OPERATIONS WITH FINDINGS

| Case  | Findings at First Operation  | Course After Cholecystectomy                           | Time Between Operations | Reasons for Second Operation            | Findings at Second Operation  | Cholecystography               | Operation   |
|-------|--|--|-------------------------|---|---|--------------------------------|---|
| E. M. | Empyema and stones   | Stones discharged through wound after leaving hospital | Six months              | Pain, jaundice, pus draining from wound | Chronic cholecystitis with empyema, gall-bladder stones, common duct stones       | "Gall-bladder not visualized." | Cholecystectomy   |
| E. A. | Chronic cholecystitis and gall-bladder stones                                  | Attacks of colic, residual pain, gall-bladder fistula  | Thirty-four months      | Pain, gall-bladder fistula              | Chronic cholecystitis with empyema, fistula, cystic duct stone                    | "Gall-bladder not visualized." | Cholecystectomy   |
| J. H. | Chronic cholecystitis, extensive adhesions from a previous abdominal operation | Symptoms not relieved                                  | Fifty-two months        | Unrelieved symptoms                     | Chronic cholecystitis   | "Gall-bladder not visualized." | Cholecystectomy   |
| W. L. | Chronic cholecystitis, gall-bladder stones                                     | Symptom-free   | 230 months              | Incisional hernia                       | Gall-bladder small, adhesions, walls thickened, no stones, yellow bile            | "Gall-bladder not visualized." | Exploratory, cholecystectomy, repair of incisional hernia |
| H. H. | Chronic cholecystitis and stones   | Improved, no colic, digestive disturbances             | Twenty-seven months     | Appendicitis                            | Chronic appendicitis, gall-bladder small, walls thickened, no stones, yellow bile | "Gall-bladder not visualized." | Exploratory cholecystectomy, appendectomy, herniorrhaphy  |

# THE SURGICALLY DRAINED GALL-BLADDER

## SUMMARY

1. Thirty-six patients were studied by cholecystography at different intervals following cholecystostomy. One, or 2.7 per cent., gave a normal response. Thirty-five, or 97.3 per cent., showed absent or impaired function.

2. Three of seven visualized gall-bladders indicated normal emptying function.

3. Eighteen patients, or 50 per cent., have remained symptom-free, yet their cholecystograms indicate impaired function. Four of these were visualized—fourteen not visualized.

4. Three had a return of symptoms severe enough to necessitate subsequent cholecystectomy.\* Two of these had stones left in the gall-bladder at their first operation.

5. Eighteen, or 50 per cent., have remained symptom-free and fourteen, or 39 per cent., are definitely improved.

6. Gall-stones were found in thirty-two patients, empyema of the gall-bladder in seven, and in six there were common duct stones. All cases of empyema and common duct stones likewise had gall-bladder stones. One had all three.

In conclusion, these findings indicate that: (1) cholecystography, being a test of function, is of no assistance in the evaluation of symptoms arising in a patient subsequent to cholecystostomy; (2) external surgical drainage of a diseased gall-bladder is not a means to a restoration of its normal function; (3) normal function of the surgically drained gall-bladder is not essential to good health and a symptom-free existence; (4) the surgically drained gall-bladder that fails to subsequently produce symptoms represents a healed-in lesion.

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<sup>7</sup> Spurling, R. G., and Whitaker, L. R.: End-results of Cholecystostomy as Shown by the Cholecystogram. *Surg. Gynec. and Ob.*, vol. xlv, pp. 463-467, 1927.

\* These patients had cholecystostomy performed elsewhere. We are greatly indebted to the members of the X-ray department of this hospital for their skillful coöperation.

# GALL-BLADDER FUNCTION

WITH SPECIAL REFERENCE TO CHOLECYSTOGASTROSTOMY AND  
THE ABSENCE OF ASCENDING CHOLANGITIS \*

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IMPRESSED by the unsatisfactory results following either cholecystostomy or cholecystectomy, I suggested cholecystogastrostomy as a compromise operation in a paper presented to the Southern Surgical Association in 1923. The observation of twenty-one cases covering a period of ten years for the longest

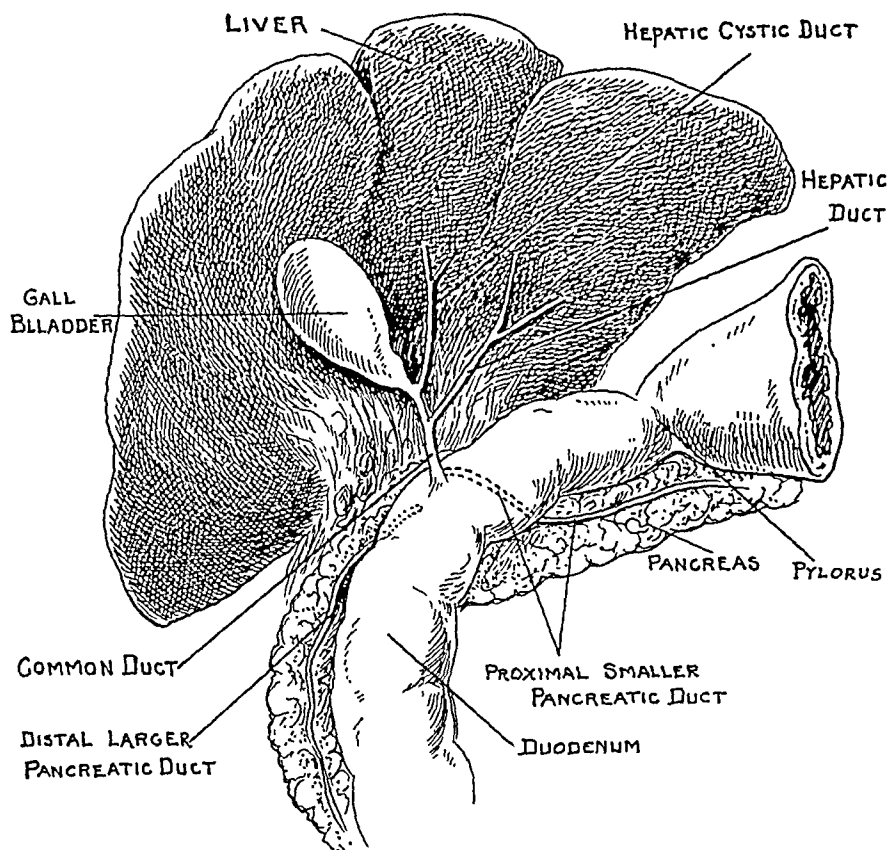


FIG. 1.—Diagrammatic outline of the liver and pancreatic ducts in the dog. Special attention to the two hepatic ducts: one to gall-bladder and one to join duct.

convinced me at that time that the bugbear of suppurative cholangitis or multiple abscess of the liver was not a sequence of this operation in the human being, although in animals, particularly the dog, it was constant. When one considers the difference in the food entering the stomach of man and that of the dog, and the consequent difference in the bacterial flora of the

\* Read before the Alabama State Medical Association, April 15, 1930.

## GALL-BLADDER FUNCTION

human stomach, which is relatively aseptic, while that of the dog is teeming with every sort of pathogenic and putrefactive bacteria, one can understand the wide divergence of necessity in the results. An even more important factor than the difference in the bacterial flora respectively of the two stomachs is the anatomic difference in that the gall-bladder in the dog through one of its two hepatic ducts communicates directly with the intrahepatic bile duct system; an open canal through which any gall-bladder infection in the dog by simple continuity involves the liver ducts.

Seven years ago, cholecystectomy was, as now, in ascendancy as the operation of choice in gall-bladder disease. One would conclude from the frequency of its surgical removal that it was not only a dispensable organ but that it was an unnecessary appendage of the liver, better out than in, being at most only a bile reservoir. These opinions in the light of our present meagre knowledge of gall-bladder function were and are grossly in error.

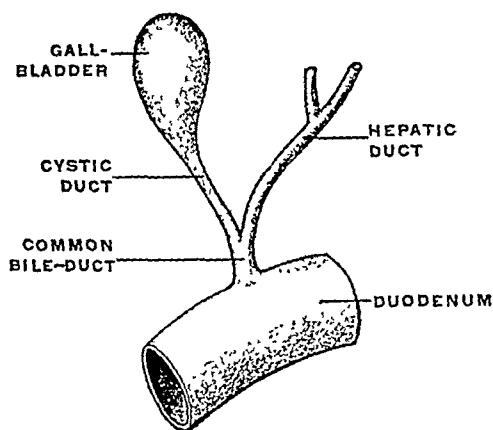


FIG. 2A.—Hepatic and cystic ducts of man.

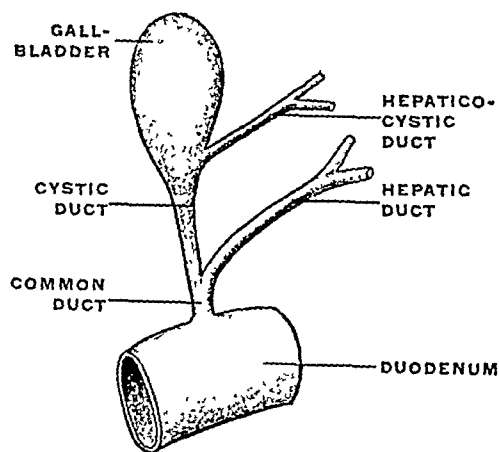


FIG. 2B.—Hepatic and cystic ducts of the dog.

At that time it was well known that in all gall-bladder infections there was a concurrent infection of varying degree of the intrahepatic tract and that the infection of the gall-bladder was but an intensified expression of the biliary duct infection. In the present state of knowledge of liver function and pathology it is just about as reasonable to do a cholecystectomy on a functioning, though infected gall-bladder, as to cut off the tail of a sick dog. Neither the urinary bladder nor the kidney is removed on account of infection nor because they happen to contain a stone, but were the urinary bladder removal easy and free from immediate danger it also would have participated in the onslaught of removing another apparently unnecessary organ of the human body. The end-results of cholecystectomy and cholecystostomy are an increasing rebuke to gall-bladder surgical treatment.

The enormous amount of research work to determine gall-bladder function other than its being a bile reservoir has resulted in valuable information. A study of its anatomy would presuppose a considerable functional activity of the gall-bladder; its profuse blood supply and the richness of its lymph follicles communicating directly to the liver cells; its ability to concentrate the bile twenty to thirty times that of liver bile; its estimated daily absorption

of bile ranging from 1200 cubic centimetres to 1500 cubic centimetres, the substances thus absorbed in addition to water are bile acids, bile pigment and lipoids, and in its absence this burden is of necessity assumed by the remaining biliary system. The gall-bladder is definitely concerned in fat metabolism, a disturbance of which causes the gall-bladder to take on more fat than its mucosa can absorb, and this excess fat is deposited on the wall of the gall-bladder as cholesterol; thousands of gall-bladders overburdened with fat metabolism have been removed because of this cholesterol deposit on the mucosa, which has been considered inaccurately a pathological condition, and described under the name of the strawberry gall-bladder. The assumption that in the human economy the gall-bladder was an unnecessary organ because

(A)

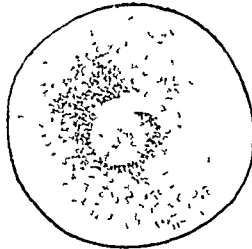


FIG 3A.—The first fold of Heister. The commencement of the neck of the gall-bladder is marked by the first fold of Heister, which is a thin semilunar membrane narrowing the lumen to less than a third of its original diameter. The orifice is eccentrically situated. (After drawing of a specimen of Doctor Sweet.)

(B)

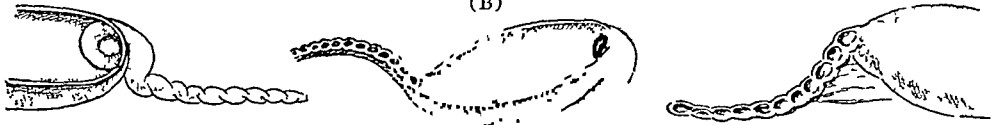


FIG 3B—Heister's illustrations of the neck of the gall-bladder and the cystic duct. They show that Heister's conception of the anatomy of these structures was clear.

it was found to be absent in many ungulates, ruminants, and rodents, that the grass and foliage feeding or the character of the food made it unnecessary is evidently in error, as in these animals it is not consistently absent; for example, in the ruminants the deer has none, while the sheep has; among the rodents, the rat is without and the mouse with a gall-bladder, the peccary has none and is a non-ruminant. It appears with more certainty that the absence of the gall-bladder is found in those animals of these groups, and some birds whose digestion is carried on continuously, or without marked interruption, a process which calls for the continuous flow of bile, there being no opportunity for storage, concentration or absorption. This variability emphasizes the morphological fact that the biliary bladder is only a modified portion of the hepatic duct system. One great surgeon says its absence is due to grass and foliage feeding, and it has been facetiously intimated that man go back to his primitive state and feed on weeds and leaves as Nebuchadnezzar of Bible lore. Would it not have been preferable for the cat and

the lion to be used as examples, as these felines have bilobed gall-bladders, which probably explains the majesty of the lion, king of beasts, and the proverbial nine lives of the cat. Cholecystectomy has been and is the most attractive feature in gall-bladder treatment. In the majority, the removal apparently has not been harmful, especially in those whose livers were capable of taking on a compensatory hypertrophy in their biliary systems, notably in the common duct which markedly dilates as a result of the state of spasm of the sphincter of Oddi following cholecystectomy—nature's plan of supplying its need for a bile reservoir. Observation of even as self-evident a fact as this is misconstrued; an instance of how far wrong such an interpretation may be is found in the statement by one observer that better drainage of the biliary system after cholecystectomy occurs on account of the increased size of the common duct which follows this operation. The most pertinent conclusion after cholecystectomy is that something better is needed, as approximately 30 per cent. have recurrence of all pre-operative symptoms and more than before; the surgical relief of which is vastly more difficult.

Ascoff states that if removability of an organ were proof of want of function, then the teeth, spleen, and many other parts of the body should be considered functionless by the same assumption.

Held and Goldbloom observe that the less dispensable an organ is the greater reserve it has, so that the liver, heart, kidneys, and lungs may become quite chronically diseased with but few signs or symptoms, even the finest functional tests failing to reveal the pathology in some instances until after the organ has broken down entirely.

Crile has stressed this sudden breaking down of the liver function following operative trauma. Extreme shock repeatedly, and death rarely, has followed withdrawing the drains after cholecystectomy. It should be noted that the dispensable organ, when it has ceased to function as a result of disease, and in the chronic types without symptoms, may menace the whole body by being either the seat of focal infection, or by direct extension of disease, and the incidence of cancer. It is here the necessity for removal is apparent and without criticism.

With reference to the emptying of the gall-bladder, there is the widest difference of opinion. The extreme from those who maintain that no bile goes from the gall-bladder through the cystic duct into the intestine to those who contend that it periodically empties its concentrated contents through the cystic duct and the sphincter of Oddi into the intestine, and that this periodic emptying depends on varying factors, the intake of food, the kind of food, diaphragmatic respiration, duodenal activity, siphonage; also drugs, notably pilocarpine, pituitrin, and magnesium sulphate. Even in cholecystography, the one assumes its reduction in size results from emptying, the other from rapid absorption; the one the different position of stones after a fat meal by emptying; the other by absorption. One observer has seen the gall-bladder contract during operation, and another is equally certain that he has never seen either contraction or elastic recoil. One maintains the activity of

the diaphragm is the main factor in emptying the gall-bladder, while another proves this an error by the gar pike which has no diaphragm, and yet its gall-bladder empties similarly to other animals with diaphragms.

Halpert has proven that the chief function of the muscular coat of the gall-bladder is to prevent overdistention and to adjust its size to its varying contents; that bile or any other fluid injected with slight pressure into one of the bile ducts above the duodenal portion fills up first the hepatic and common

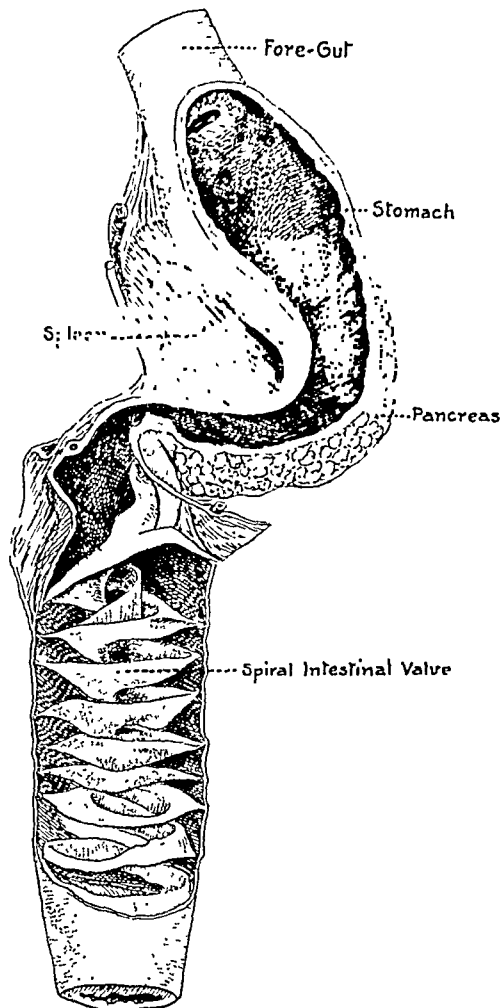


FIG. 4.—Spiral intestinal valves in the dogshark.

ducts, then the cystic duct, and finally the gall-bladder. Fluid or bile from the gall-bladder does not enter the duodenum however until the gall-bladder becomes greatly distended. If there is a small hole in one of the bile ducts, then the filling of the gall-bladder from the ducts does not occur, the fluid passing through the hole, none going to either gall-bladder or duodenum. A hole in the gall-bladder, though very small, even a needle prick, permits abundant escape of bile indicating pressure within the ducts. Halpert has also demonstrated rhythmic contractions of the gall-bladder occurring from

## GALL-BLADDER FUNCTION

one to three per minute in frequency, having from 2 millimetres to 46 millimetres with a displacement of from 0.1 to 2.3 cubic centimetres of Locke's solution. Stasis in the gall-bladder is due to an abnormal composition of the bile from a disturbed function of the liver or to an altered power of absorption within the gall-bladder mucosa, therefore the processes leading to stasis may be either in the gall-bladder or in the liver or in both the liver and the gall-bladder.

The study of these disturbances of function or of altered physiologic activity common to both the gall-bladder and liver are cited and stressed as

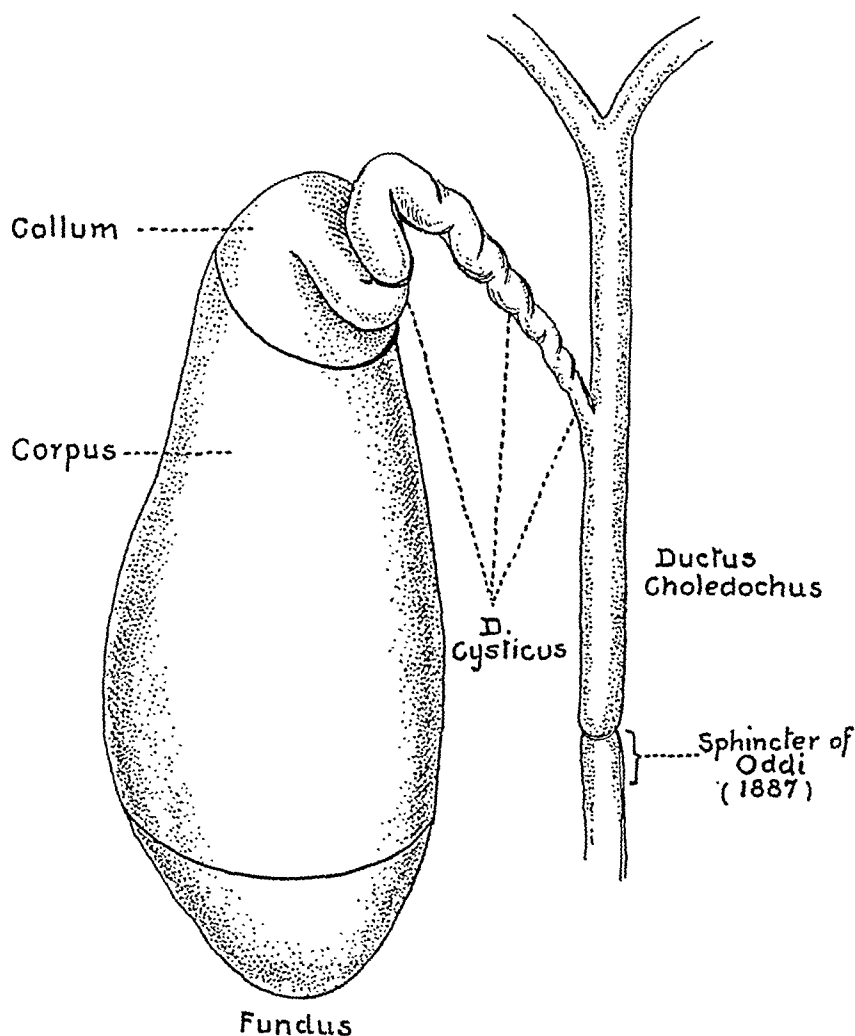


FIG. 5.—Diagram of the extrahepatic bile ducts and the gall-bladder. They form a Y-shaped communicating vessel of which the ductus choledochus is the stem, the common hepatic duct the one branch and the cystic duct the other. (After B. Halpert, *Arch. of Surgery*.)

added proof of liver and gall-bladder interdependence physiologically and pathologically, that the incidence of infection is common and concurrent in both, and of the necessity of recognizing the gall-bladder, biliary ducts and liver as a unit in future research.

Under Crile's electrochemical hypothesis, cholecystogastrostomy should balance the potential of the acid and the alkali reserve in the system. In the pathology and healing process of gastroduodenal ulcers, Goyena stresses the great importance of the equilibrium of the acid and alkaline factors of the organism.



A perplexing confusion, even chaos, exists in experimental research on this subject; some failures, few though they be, are from faulty methods and illogical deductions, which confuse rather than clarify. With greater frequency, and even more disturbing, are the contradictory results obtained by equally efficient research workers, and here it seems that there has been entirely left out of the equation the difference in the physiologic and pathologic status of the varying types of vertebrates, the difference between either the chemical secretion or the bacterial content of the same organ in different animals, of the state of health, or of the functional activity differing as it does in different individuals of the same species, and under varying conditions in the same individual of any species at different periods of time. Without a proper understanding and correct evaluation of those fundamental differences, not only of types but of conditions in the same type, disparity in result is a logical sequence.

The anatomic structure of the cystic duct permits an easy inflow and a difficult exit of bile, some observers contending that no bile passes from the gall-bladder through the cystic duct. The Heisterian folds of mucosa produce one-way valves and are competent to the water test when the gall-bladder is filled. It is interesting to note that the spiral folds such as are found in the cystic duct are also present in a modified form in the valvulae conniventes and the crescentic folds of the large intestine. Similar spiral mucus folds are encountered in the higher vertebrates, being especially well developed in the large intestine of rodents, ruminants, some fishes, and birds. The S-shaped turn at the neck of the cystic duct and the conical shape of the duct itself, narrowing as it runs its course to join the hepatic duct, is another factor interfering with the passage of the bile from the gall-bladder. These anatomic structures fulfill the same purpose after cholecystogastrostomy that the oblique entrance of the common bile duct through the duodenum and the ureter through the bladder does in inhibiting ascending infection. The rôle of ascending infection in both the kidney and bile tracts is a negligible factor; it is generally recognized and accepted that infections in the biliary and urinary system for the greater part are hæmatogenous in origin.

Choledochoduodenostomy is a standard surgical procedure done under certain definite indications, and attention has not been called to the danger of ascending infection as a sequence nor have any cases been reported of the incidence of cholangitis or suppurative hepatitis following this operation, and in this procedure there is a direct communication between the biliary duct system and the duodenum.

Attention is again called and emphasized in regard to the failure of research workers in animal experimentation in recognizing the difference in the anatomic structure of the human gall-bladder and that of the dog, the most used animal in experimental research in gall-bladder and liver surgery. There is no parallel or similarity in the operation of cholecystogastrostomy on the dog and human being as a proof of secondary ascending infection, cholangitis or multiple abscess of the liver, etc., since the dog has the

## GALL-BLADDER FUNCTION

hepaticocystic duct, an accessory biliary canal, a direct communication between the gall-bladder of the dog and his intrahepatic biliary ducts, which is not found in the human being. The fact that the dog has another hepatic duct similar to man which joins with the cystic duct to form the common bile duct perhaps has caused this main factor of a direct communication between the gall-bladder and the intrahepatic biliary ducts of the dog to have been overlooked, and to have been left out of the deductions from such work; it certainly has not been mentioned in the many papers on this subject coming under my notice. There is still another anatomic difference between the dog in that the pancreatic and the common bile ducts do not unite—the dog having no Ampulla of Vater—but enter the duodenum below the entrance of the common bile ducts by two canals each the prototype of Santorini and Wirsung respectively, and are called the proximal smaller and distal larger pancreatic ducts.

THE ABSENCE OF AN ASCENDING INFECTION IN HUMAN BEINGS IS ACCOUNTED FOR BY

1. Anatomic structure of the cystic duct.
  - a. Heisterian folds of the mucosa, producing one-way valves which are "competent to the water test."
  - b. S-shaped curve of neck of cystic duct.
  - c. Conical shape of duct narrowing to a very small opening at its junction with the hepatic duct.
  - d. Fundus of the gall-bladder being the most dependent part of the biliary duct system, lower than the Ampulla of Vater.
2. The constant intra-biliary duct pressure.
3. Relatively sterile food and low grade bacterial gastric content.

### INDICATIONS FOR CHOLECYSTECTOMY

1. Non-functioning gall-bladder.
  - a. Atrophic or contracted gall-bladder.
  - b. Irreparable cystic duct occlusion.
2. Cancer of gall-bladder.
3. Gangrenous cholecystitis.

### INDICATIONS FOR CHOLECYSTOGASTROSTOMY

1. Common duct obstruction in the poor surgical risks.
2. Residual hepatic duct stones.
3. Chronic obscure jaundice.
4. Extrahepatic duct obstruction.
5. Perforation of the gall-bladder.
6. Perforated stomach ulcer.
7. Gastric and duodenal ulcer.
8. Jejunal gastro-enterostomy ulcers.
9. Acute pancreatitis.
10. Acholia following cholecystostomy.

### INDICATIONS AND CASES OPERATED ON, JAN. 1, 1926 TO JAN. 1, 1930

|  |   |
|--|---|
| Cholelithiasis with colic .....                  | 6 |
| Cholelithiasis and empyema of gall-bladder ..... | 2 |
| Suppurative cholelithiasis with jaundice .....   | 2 |
| Suppurative cholecystitis with jaundice .....    | 3 |
| Rupture of gall-bladder (Cholecystitis) .....    | 1 |

## FRANCIS G. DuBOSE

|  |   |
|--|---|
| Acute pancreatitis with jaundice .....     | 1 |
| Chronic obscure jaundice and ascites ..... | 1 |
| Gastric ulcer .....                        | 4 |
| Duodenal ulcer .....                       | 3 |
| Obstructive jaundice                       |   |
| Carcinoma of pancreas .....                | 1 |
| Carcinoma of liver .....                   | 1 |

### CASES PREVIOUSLY REPORTED

|                                   |    |
|-----------------------------------|----|
| Operations 1912 to 1926 .....     | 32 |
| Operative recoveries .....        | 30 |
| Recurrence of symptoms .....      | 3  |
| Re-operation for recurrence ..... | 3  |
| Cured by re-operation .....       | 3  |

### CASES IN THIS SERIES

|                               |           |
|-------------------------------|-----------|
| Operations 1926 to 1930 ..... | 25        |
| Mortality .....               | 0         |
| Recurrence of symptoms .....  | 0         |
| Total cases .....             | 57        |
| Total mortality .....         | 2 or 3.5% |
| Total recurrence .....        | 3 or 5.2% |

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## CHOLECYSTECTOMY WITHOUT DRAINAGE\*

BY RUSSELL S. FOWLER, M.D.

OF BROOKLYN, N. Y.

THE writer made a study of this subject in 1924, at that time having omitted drainage in eighty-one cases.† Since then drainage has been omitted in other cases bringing the total up to 240 cases. Of these cases forty-six were males, 194 were females.

All cases showed evidence of chronic inflammation. They have been classified, however, according to the most prominent aspect present at the time of operation.

|  |            |
|--|------------|
| Cholecystitis catarrhalis acuta .....    | 43 cases.  |
| Cholecystitis catarrhalis chronica ..... | 18 cases.  |
| Cholecystitis acuta .....                | 35 cases.  |
| Cholecystitis chronica .....             | 144 cases. |

Adhesions were present in all cases, varying from slight adhesions of the ampulla to the duodenum to extensive adhesions involving the fundus as well. Enlargement of the gland at the upper portion of the cystic duct was always present. Microscopic section was made in each case.

Stones were present in about one-half of the cases. Whether stones are present or not is immaterial for they are but one of the ways in which the inflammation expresses itself.

Additional lesions were present in some cases; several of these were of special interest, one a curious lesion of the pancreas which showed a uniformly hard and large pancreas with yellow shot-like infarcts; one a cystic disease of the liver in which the liver presented the appearance of being filled with shot, there being numerous small black shot-shaped and shot-feeling areas which on incision yielded clear serum; one a case of sclerosis of the pancreatic artery but without general arteriosclerosis; one a case operated early in pregnancy; three cases showed papilloma of the gall-bladder; one a calcification of the gall-bladder; one a biliary sinus.

Additional operations were done in many cases. In 177 cases appendectomy was done as well as cholecystectomy. One hundred and seventy-three of these cases showed chronic inflammation, three subacute inflammation, and one an acute inflammation. It is my practice to take out the appendix in all except the very acute gall-bladders. In forty-five cases the appendix had been removed at a previous operation. In eighteen cases no attempt was made to remove the appendix. In some cases associated operations were done for the following lesions: Nephroptosis, four; epigastric hernia, one; umbilical hernia, three; inguinal hernia, two, one case bilateral; hepatosis, one; cirrhosis of liver, one; sebaceous cyst, one; duodenal ulcer,

\* Read before the Brooklyn Surgical Society, November 6, 1930.

† Cholecystectomy without drainage. *Am. Jour. of Surgery*, New Series, vol. v, No. 1, pp. 8-14.

five; diastasis of rectus muscles, one; hæmorrhoids, one; ovarian cystoma, two; Mullerian cyst, one; salpingitis, two; cystic ovary, two; prolapsus uteri, five; retroversion, seven; cystocele, one; lacerated cervix, two; lacerated perinæum, nine; adhesions (other than gall-bladder adhesions) resulting from previous operations, omental, fifteen; intestinal, three; old peritonitis, two; adhesions about appendix, three; adhesions about ovary, two.

*Hospitalization.*—The longest stay in the hospital was seventy-eight days, a case of advanced myocarditis. The shortest stay was thirteen days. Omitting the deaths, the average stay was sixteen days. It is my practice to keep patients in the hospital until they are strong enough to care for themselves; occasionally a patient will insist on going home as soon as he is able to walk about, and more rarely, some will wish to overstay their time.

*Wound Healing.*—Six of the 240 cases are omitted from consideration in this regard as death occurred within ten days post-operatively, leaving 234 cases for consideration. In no case was there any escape of bile through the wound, nor any bile discernible in the wound discharge during any of the wound complications.

Primary union, 223 cases. Wound complications, eleven cases classified as follows: Serum, trifling in amount, one case; serum and later pus, two cases; more pronounced infection but not severe, four cases; hæmatoma, superficial, one case; deep, one case; wound rupture, two cases.

*Post-operative Complications.*—Cases considered 240, of which eight died. One hundred and eighty-four cases showed no untoward symptoms. In addition to the wound complications already noted there occurred twenty-eight respiratory complications: Sore throat, three cases; slight cough, seventeen cases; pleurisy, one case; pneumonia, seven cases, one of which occurred three days after the patient left the hospital. Vomiting severe enough to be noted, six cases, one of which showed vomiting of blood, a case in which a gastro-enterostomy had been done for associated duodenal ulcer and blood was noted in the vomitus once; of the six cases one vomited so excessively as to cause wound rupture. Other complications: Phlebitis, three cases; involuntary defecation, one case; chill following catheterization, one case; prolonged and severe shock, one case; abscess in buttock, one case. Four cases subsequently developed ventral hernia.

Of the deaths one was a sudden death without premonitory symptoms, the patient being found dead in bed eight days post-operatively. This was a case of chronic cholecystitis without stones and subacute appendicitis in an otherwise healthy individual. Three cases, two chronic and one acute cholecystitis, died of pneumonia, two on the fourth day, one on the seventh day post-operatively. One acute cholecystitis died of shock and pneumonia, two days post-operatively. One chronic cholecystitis developed intestinal paresis for which an enterostomy was done, succumbing on the sixth day post-operatively. This case showed no evidence of bile leakage or peritonitis, but did have an enterospasm. One chronic cholecystitis died of wound rupture and its accompanying shock on the eleventh day after the original operation. One chronic cholecystitis died of pneumonia twenty-

two days post-operatively, a very obese woman who had a most stormy course with final wound rupture. On resuturing the wound no peritonitis or escape of bile, or lesion other than that caused by wound rupture was discovered. The writer thought there was an obscure lesion of the pancreas, perhaps a beginning carcinoma, but with this the consultant entirely familiar with all the facts could not agree.

*Temperature Range After Operation* (234 cases considered).—The average lowest and highest temperature for each of the first three days post-operative was: first day, lowest temperature, 99.3°; highest, 100.8°; second day, lowest temperature, 99.1°; highest, 100.3°; third day, lowest temperature, 98.7°; highest, 99.8°. The average of fifty temperatures of cholecystectomy with drainage was 99° F. for fourteen days post-operative. This temperature study was made in connection with the use of the Fowler position after operations upon the upper abdomen. It was found that the temperature average was lower in cases in which the Fowler position was used. This point was utilized in a paper read before the International Congress in London in 1914, the study showing that infections through the lymphatics are less prone to occur after operations upon the upper abdomen if the patients are placed in the Fowler position.

The temperature range does not seem to be influenced to any great extent by the omission of drainage. As a matter of fact the temperature after cholecystectomy depends upon two factors, the character and amount of infection present, and the delicacy with which the operation is performed.

*Final Results.*—Eight cases died, 3 1/3 per cent. Seventeen cases have not reported since they were discharged from the hospital; 196 cases report themselves well for periods varying from three months to eight years after operation; nineteen cases reported symptoms of one kind or another at periods varying from three months to seven years post-operatively.

I think we should omit from consideration all cases in which less than a year has passed as I find that many cases have symptoms of one kind or another, mostly up to three months after operation, though sometimes as long as a year. These symptoms take the form of a mild indigestion, loss of appetite and associated symptoms due to the condition of the liver itself, as in so many gall-bladder cases there is passive congestion with its accompanying inability to care for certain foods and large quantities of food. I have not worked out the exact number of cases which require instructions in diet, and more particularly limitation in the amount of food taken, but, roughly speaking, would estimate the percentage at about 25. The liver in gall-bladder disease cannot care for an excessive amount of food; overeating must be warned against. Cases presenting slight symptoms yield readily to dietetic measures.

Omitting the cases in which the reports are less than a year, eighty-one cases (of which seventy-six report themselves as well and five report themselves as having mild symptoms) and those in which no report has been received, seventeen cases, and the eight deaths, leaves 134 cases of which 120 or 89.6 per cent. report themselves well from one to eight years post-

operatively; eight cases or 5.9 per cent. report mild symptoms from one to four years post-operatively; six cases or 4.5 per cent. report either severe symptoms or no improvement one to seven years post-operatively.

*Comparison of Ectomy with and without Drainage.*—Wound infection seems to be at least as common with drainage as without. The same may be said of hæmatoma. The writer's impression is that there is a slight difference in comfort in favor of those cases which are not drained. Comfort following operation bears a distinct relation to the skill used in operating and in caring for the wound afterward.

As to the final result, we have for comparison 543 cases of cholecystectomy with drainage, of which fifteen died, a mortality percentage of 2.7, compared with 240 cases of cholecystectomy without drainage of which eight died, a mortality percentage of  $3\frac{1}{3}$ . The mortality percentage is, of course, in favor of cholecystectomy with drainage. This is the more marked when we consider that cholecystectomy without drainage is done in the simpler cases.

Comparing the late results we have 406 cases of cholecystectomy with drainage with reports available one year or more post-operatively. Of these 365, or 94.8 per cent., reported themselves as being well; ten cases, or 2.5 per cent., reported themselves as having mild symptoms; eleven cases, or 2.7 per cent., reported themselves as having severe symptoms.

Comparing the above percentages with a similar analysis of 134 undrained cases of which reports are available from one to eight years post-operatively we have a marked difference in each class in favor of the cases which have been drained, and this again is the more remarkable as the drained cases undoubtedly showed more advanced pathology.

In view of the favorable statistics which this series of cholecystectomy with and without drainage for acute and chronic gall-bladder disease presents 783 cases with 23 deaths, a mortality percentage of less than 3 per cent., the writer wishes to say that while the common duct was explored in practically every case, this series does not include cases in which drainage of the common duct by T tube was done. Exploration of the common duct through the stump of the cystic duct does not seem to increase the mortality. Choledochostomy, however, with incision of the duct, removal of stones, cleansing of the duct and T-tube drainage raises the mortality about 1 per cent. This is not to be wondered at as such cases, having had their infection for a long time, show more damage to the liver.

In the last thousand cases of cholecystectomy, choledochostomy with T tube was necessary in ninety cases of which eleven died, a mortality percentage for cholecystectomy plus choledochostomy of 12.2 per cent.

When we find, as we do in this study, that in a series of 240 cases the percentage of deaths is greater than in a very much larger series of drained cases more severe in character, and when we find that in the analysis of the final results the drained cases show a considerable superiority in percentage of cures over the undrained, we must conclude that in spite of the temptation not to drain, it is wiser to drain.

## SPLENECTOMY FOR HÆMORRHAGIC PURPURA OF CHILDREN\*

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FROM THE MAYO CLINIC AND THE MAYO FOUNDATION

THE removal of any organ from an extremely young child is a formidable procedure under any circumstances, and often is not successful. Nevertheless, the literature is replete with reports of extremely hazardous procedures, such as resection of the colon for intussusception, operations on the stomach for obstruction, and even removal of kidney or spleen under disadvantageous circumstances, with successful results. The necessity of performing splenectomy on a child aged four years prompted us to review the literature on this subject. We found that the spleen had been removed with favorable results from two other patients slightly younger than the one we had operated on. The subsequent satisfactory improvement in our case seemed to warrant a report of the case in detail.

REPORT OF CASE.—A boy, aged four years and two months, was brought to the clinic May 27, 1930. There was no history of "bleeders" in the family. During the last year the patient had had nosebleed, and bleeding from the gums. He also had had purpuric eruptions over the body; at times they had been diffuse, covering almost the entire body. The patient was easily bruised, and cut areas would bleed for several minutes. Tarry stools had been noted; the last hæmorrhage had occurred two months before his admission to the clinic.

General examination revealed anæmia graded 2, and large, bluish spots on the legs, arms and ears. The mucous membranes were pale and covered with petechial spots, as were the tonsils, which were small. The spleen was palpable, graded 1. The liver was enlarged, graded 2, and palpable below the costal margin.

The urine was acid in reaction; it did not contain albumin or sugar. The specific gravity was 1.030. The microscopic examination was negative. May 28 the hæmoglobin was 53 per cent.; erythrocytes numbered 3,930,000; leucocytes, 3,900; lymphocytes, 41 per cent.; large mononuclear leucocytes, 2 per cent.; transitionals, 3 per cent.; neutrophils, 46 per cent.; eosinophils, 3 per cent.; and recticulated cells, 0.9 to 0.8 per cent.; anisocytosis and poikilocytosis were present, and there was slight basophilic stippling and mild polychromatophilia. Platelets numbered 30,000 to 40,000. The coagulation time was fourteen minutes (Boggs); the bleeding time was one hour on one occasion, and forty minutes on another. May 30 the calcium coagulation time was seven minutes; there was no retraction at the end of twenty-two hours. The blood was in group 4. At this time platelets could not be found. Prothrombin time was 3 drops in ten minutes, 5 drops in twelve minutes, 7 drops in twenty minutes, 2 drops in ten minutes, 4 drops in twelve minutes, 6 drops in fifteen minutes, and 8 drops in twelve minutes. Erythrocytes numbered 4,260,000 and leucocytes 3,800. A röntgenogram of the thorax was negative. A diagnosis of hæmorrhagic purpura was made. The patient was in good condition and transfusion of blood was not necessary.

Splenectomy was performed June 6. The spleen, which was twice normal size, was removed without difficulty. The liver was larger than normal and had sharp edges.

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\* Submitted for publication October 28, 1930.



The gall-bladder was normal. The spleen was firm and pink; it weighed 60 grams and there was an increase in the number of malpighian bodies.

The platelets rose to 68,000 soon after operation. The erythrocytes numbered 3,520,000; the coagulation time was six minutes, and the bleeding time, twenty-five minutes. The hæmoglobin was 40 per cent. Platelet counts were made daily and the results were as follows: 68,000, 48,000, 34,000, 24,000, 28,000 70,000, and 94,000.

Convalescence was uneventful except for slight bleeding from the nose. When the patient was dismissed from observation, June 19, the platelet count was 84,000, the hæmoglobin was 60 per cent., the erythrocytes numbered 3,500,000, and the leucocytes numbered 4,900. The coagulation time was five minutes, and the bleeding time was ten to twenty minutes. The purpuric spots had disappeared. There was no bleeding from the gums or any other source. July 29, 1930, the patient's mother wrote that the child was doing nicely; there was no evidence of bleeding.

*Diagnosis.*—Hæmorrhagic purpura indicates the spontaneous extravasation of blood into or under the skin and mucous membrane of the body. It is a symptom common to many diseases of diverse character and is not a disease in itself. Its etiology is uncertain but the condition, characterized by bleeding and associated with marked reduction in blood platelets and disturbance in blood coagulation, is thrombopenic purpura. The condition was first distinguished from other forms of hæmorrhagic disease by Werlhof, in 1781, and is sometimes even now termed "Werlhof's disease." According to Clough, it is probably dependent on constitutional abnormality of the bone marrow and in some cases there may be a hereditary tendency. The work of Duke shows the close relationship of the platelets to the bleeding time and clot retractility. Some authors stress the close parallelism between the number of platelets and the clot retractility much closer than that between the platelets and bleeding time. Koster noted the increased phagocytosis of platelets by endothelial cells. He also noticed dysfunction in the formation of the platelets and increased permeability of the capillary walls.

The primary cause of hæmorrhagic purpura may be an infection or a toxin which affects the spleen or other lymph tissues, or it may be due to some abnormality of the bone marrow. Other factors, such as increased permeability of the capillary walls, some interference in the production of normally functioning platelets, and increased destruction of platelets may occur. On examination of patients suffering from this condition, one usually finds only bleeding and anæmia.

A good history and a study of the blood will clinch the diagnosis. Data concerning the blood are: (1) increased bleeding time, (2) decreased platelet count, (3) a non-retractile clot, and (4) normal or slightly increased coagulation time. There is positive reaction to the Rumpel-Leeds test. The blood picture during periods of bleeding shows outstanding reduction in blood platelets, usually less than 60,000, and sometimes less than 10,000. The blood may show evidences of post-hæmorrhagic secondary anæmia which may become extreme. There is usually regeneration of erythrocytes, and polychromatophilia may be present. The coagulation time may be normal or slightly increased. The clot is abnormal in its failure to retract in the

usual manner; the non-retractility is due to the lack of blood platelets. In hæmophilia there is a normal platelet count, a normal bleeding time, and prolonged coagulation time, but there are not many diseases that may be mistaken for hæmorrhagic purpura, especially if one studies the blood.

The chief indications for splenectomy in hæmorrhagic purpura have been pointed out by Giffin, Reuben and Clamon, Gregory, and others. After a correct diagnosis has been made, one is justified in performing splenectomy.

The reticulo-endothelial system seems to play a part in hæmorrhagic purpura. Aschoff described this system many years ago. One particular function of it is to devour the used-up erythrocytes, leucocytes, and the platelets of the circulating blood, and to metabolize them. Such cells are found in the sinuses of the lymph-nodes, the blood sinuses of the spleen, the capillaries of the lobules of the liver, and the bone marrow. Inasmuch as the reticulo-endothelial cells get rid of the jaded or excessive blood platelets, it is logical to assume that in a disease such as hæmorrhagic purpura, in which a low platelet count is a prominent feature, some part of this system is overactive. If the overactive cells are largely limited to the spleen, its removal would promise immediate good and probably permanent results. The bleeding time is prolonged and is directly proportional to the degree of reduction of platelets. There is diminished capillary resistance which is shown by the Rumpel-Leeds test. This test is carried out by applying a blood-pressure cuff to the arm at the mean blood pressure for five minutes. The test is positive if, within a few minutes after removal of the cuff, purpuric spots appear on the arm below the cuff. Profuse spots and spots of large size (1 centimetre in diameter) are almost pathognomonic of hæmorrhagic purpura.

This condition may go on for some time, or death may occur from hæmorrhage within a few weeks of the onset. The first attack usually subsides after one to three months and there may never be recurrence of bleeding. In most cases, the condition persists and runs a remittent or intermittent course. Remission is usually associated with a rise in platelets. Remission may last for a few weeks or for many years. During these intervals there is often a definite reduction in platelets, but not to the extent of causing bleeding. Purpuric eruptions are absent in some cases. The bleeding may be limited to a single source, for instance, the nose or bowel.

Differential diagnosis depends on the blood changes which are characteristic of hæmorrhagic purpura as follows: (1) diminished platelets, (2) prolonged bleeding time, (3) normal coagulation, (4) non-retractile clot, and (5) the reaction to the Rumpel-Leeds test.

The relation of decreased blood platelets to hæmorrhagic purpura is well recognized. Whether the decrease in blood platelets is due to the failure of the megakaryocytes of the bone marrow to form new platelets or to overactivity of the reticulo-endothelial cells to destroy them is still an unsettled question. The general opinion would seem to favor the theory that the blood platelets are formed in normal numbers but are destroyed by overactive

phagocytosis in the spleen and other parts of the reticulo-endothelial system. Therefore, the severity of the bleeding in hæmorrhagic purpura would seem to depend on: (1) thrombocytosis; (2) the extent to which certain cells of the reticulo-endothelial system engaged in thrombocytosis are distributed in the spleen, liver, bone marrow, and lymph-nodes, and (3) permeability of the capillaries to the circulating blood. The third of these factors has not been thoroughly investigated.

*Treatment.*—Unquestionably, splenectomy is the most satisfactory treatment for purpura of this type. Splenectomy for the condition has been performed at The Mayo Clinic in forty cases, with results which obviously justify the procedure as the wisest therapeutic measure (tabulation). The earlier the operation is performed in the course of the disease, the better are the results. It may be asked whether operation is contra-indicated in the

## TABULATION

*Results in forty cases of hemorrhagic purpura subjected to splenectomy at The Mayo Clinic*

| Age, years | Cases | Male | Female | Results (no deaths) |      |      |
|------------|-------|------|--------|---------------------|------|------|
|            |       |      |        | Good                | Fair | Poor |
| 0-16.....  | 12    | 3    | 9      | 12                  |      |      |
| 16-30..... | 18    | 6    | 12     | 15                  | 3    |      |
| 30-50..... | 9     | 3    | 6      | 8                   |      | 1    |
| 50-60..... | 1     | 1    |        | 1                   |      |      |
| Total..... | 40    | 13   | 27     | 36                  | 3    | 1    |

acute stage of the disease, that is, when the patient is having hæmorrhages. In such a case, it would probably be better to give two or three transfusions to see if the patient improves. If the bleeding continues, one would be justified in proceeding with splenectomy. On the other hand, if the patient improves following blood transfusions, one should wait until the risk of operation is lessened before performing splenectomy. Whipple and Spence have stated that splenectomy is definitely contra-indicated in acute cases, and Giffin, Reuben and Clamon, and others have stated that the acuteness of the condition is not a safe guide. There are patients who no doubt do better after having received pre-operative treatment, such as transfusions and intravenous injections of calcium lactate, or calcium chloride, but this depends entirely on the case and a study of the blood. If the platelet count is extremely low, and the bleeding time is very much prolonged, in the presence of marked secondary anæmia, it is advisable to give transfusions of blood and to use any other precautionary measures that may help in a particular case. The only effective method of controlling bleeding in severe cases, according to Clough, is transfusion of blood. Relief is usually temporary, lasting from three to four days, which is the probable average life of the platelets. In some cases unaltered blood seems to be more effective than citrated blood. Preparations, such as serums, thromboplastic substances, calcium salts, and so forth, usually have little if any effect.

It is the belief of Giffin and Holloway that splenectomy is necessary in order to obtain sustained relief. In almost all cases bleeding stops promptly and there is usually a marked rise in the number of platelets. In a few weeks or months the platelet count again falls but in most cases bleeding does not occur. It is not certain just how removal of the spleen stops bleeding. Clough stated that the spleen possibly has been actively destroying platelets or that it has been exercising an inhibiting influence over the formation of platelets in the bone marrow. This part of the question is unsettled. Evans found that there is a rise in platelet count following splenectomy for such different causes as trauma, acholuric jaundice, and splenic anæmia.

*Prognosis.*—The prognosis is good. The forty patients on whom splenectomy was performed at The Mayo Clinic are living and in good health. There is no tendency to bleeding. It seems that the best results are obtained in cases of children and that the prognosis is more favorable when the spleen is removed early in the course of the disease. The greatest value in the study of prognosis is the summarizing of end-results. This has been carefully done by such men as Williamson and Spence who found that the prognosis and end-results were good.

An important point in diagnosis, treatment and prognosis is to decide whether the disease is chronic and recurrent, or whether it is the acute fulminating type. The chronic type is promptly and permanently cured by splenectomy. There is an immediate rise in platelets and a return of the bleeding time to normal. The acute type does not respond satisfactorily to such a procedure. The condition may come on suddenly without any history suggestive of it. Repeated transfusions may be necessary. One patient at The Mayo Clinic was given twelve transfusions in forty days. In view of the fact that splenectomy cures, it is evident that the major disturbance of the reticulo-endothelial system is localized in the spleen. In Whipple's review of eighty-one cases, seventy-three were of the chronic type, in six of which death occurred, and eight were of the acute type, in seven of which death occurred.

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# END-RESULTS IN RADICAL OPERATIONS FOR CARCINOMA OF THE PERIAMPULLAR REGION OF THE DUODENUM\*

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ALTHOUGH most authors agree in that carcinoma of the periampullar region is a rare disease, a sufficient number of operations have been done both with and without operative recovery to justify a careful analysis of the end-results to be expected. Despite all our newer means of diagnosis, this disease is still one primarily diagnosed either at operation or autopsy, and the suddenness with which the surgeon is confronted by the tumor mass demands some familiarity with the knowledge of operative risk, end-results and results to be expected by means of palliative operations and radical procedures. Because of the key situation very small tumors must early produce symptoms of blockage of the common duct, with or without blockage of the pancreatic passages as well. Because of this and because of the notoriously late metastasis, this tumor should be one most amenable to surgery, were it not for several complications. First of all, the operation, as has so many times been stated by other writers, must be done on a jaundiced patient. Thoroughly as this patient may be prepared by intravenous glucose, calcium or sera, the risk of hæmorrhage still remains second only to the risk of liver shock. Mortality of any operative procedure except an exploratory incision ranges from 30 per cent. to 70 per cent. depending on duration of jaundice and the type of operation performed.

Thus in the last few years, with all possible preparation, the following table represents the operative mortality reported in the literature. All cases are radical resections or stages thereof.

TABLE I

| Author            | Operative Death | Survived      |
|-------------------|-----------------|---------------|
| Busch.....        | 0               | 1             |
| Hingst.....       | 2               | 1             |
| Bruning.....      | 2               | 1             |
| Klinkert.....     | 0               | 1             |
| Clar.....         | 0               | 1             |
| Murgoci.....      | 2               | 0             |
| Denks.....        | 4               | 1 (2 cases Sa |
| Van Remyense..... | 0               | 1             |
| Van Ardenne.....  | 0               | 1             |
| Schofield.....    | 1               | 0             |
|                   | —               | —             |
|                   | 11              | 8             |

Of these operative deaths, two had post-operative hæmorrhage, four had liver shock, three died of cardiac failure and one of general sepsis from

\* Read before the Philadelphia Academy of Surgery, November 3, 1930.

cholangitis. Thus the gross mortality of cases reported within recent years is still 58 per cent. Of the fifty-nine cases reported before this time by Cohen and Colp, twenty-four died an operative death in the primary operation, both radical and palliative. In their own series of eight cases, six died an operative death, or a gross operative mortality, including their own report, of 45 per cent.

The end-results of any radical operation for carcinoma must receive a critical examination, especially in the face of a primary high mortality. This is self-evident, since there is fundamentally little value to any patient if the relief obtained by operation is neither complete nor lasting.

The number of patients dying within one year, from either rapid advance of the primary growth or of wide metastasis, seems to be relatively large when one considers that this tumor is supposedly slow in growth and late to metastasize. One must consider, however, that in the cases early reaching their termination, metastasis was occasionally present at operation, and certainly the average had a much longer history of complaints. After operation the patient is in every case relieved and usually permanently, of a most irritating and bothersome symptom—the itching of obstructive jaundice. A careful analysis of individual case reports in the literature demonstrates also the long intervals of freedom from pain or symptoms of any sort in successfully operated cases. Death usually comes about by more or less painless inanition, although pain can occasionally be a severe factor.

Aside from the palliation of symptoms, what chance does the patient have of actual cure, following radical operation? This is the question of most vital importance to any surgeon confronted with carcinoma in any region. Many authors have reviewed the literature in the past, the most complete reviews being found in the reports of Cohen and Colp, Fulde, and Hingst. Busch in 1928 made a complete analysis, reporting nine cases which lived one year or more. To this we have added more recent reports as follows:

TABLE II

|                    | No. of years | Reported by    |
|--------------------|--------------|----------------|
| Körte.....         | 22           | Busch          |
| Lewis (Kelly)..... | 9            | Lewis          |
| Oehler.....        | 6            | Busch          |
| Van Remyne.....    | 6            | Klinkert       |
| Van Ardenne.....   | 5            | Klinkert       |
| Hingst.....        | 5            | Hingst         |
| Clar.....          | 5            | Clar           |
| Oliani.....        | 4            | Cohen and Colp |
| Tenani.....        | 3            | Tenani         |
| Morin.....         | 2½           | Busch          |
| Novarro.....       | 2            | Busch          |
| Abell.....         | 2            | Busch          |
| Fulde.....         | 2            | Fulde          |
| Busch.....         | 1            | Busch          |
| Homans.....        | 1            | Homans         |
| Propping.....      | 1            | Busch          |

Thus there are a total of sixteen cases of eighty-one cases reported who lived more than one year, about two-thirds of which were still living and well when reported. The procedures in cases living four years or more were as follows:

TABLE III

| Author           | Procedure                         | Lived | Status       |
|------------------|-----------------------------------|-------|--------------|
| Körte.....       | Transduod. Excis. Reimplant. C.D. | 22    | Symptom-free |
| Lewis.....       | Transduod. Excis. Reimplant. C.D. | 9     | Symptom-free |
| Oehler.....      | Transduod. Excis. Reimplant. C.D. | 6     | Symptom-free |
| Van Remyse.....  | Transduod. Excis. Reimplant. C.D. | 6     | Unknown      |
| Van Ardenne..... | Transduod. Excis. Reimplant. C.D. | 5     | Unknown      |
| Hingst.....      | Cholecystoduodenostomy            | 5     | Died         |
| Clar.....        | Transduod. Excis. Reimplant. C.D. | 5     | Died         |
| Olani.....       | Transduod. Excis. Reimplant. C.D. | 4     | Symptom-free |

It is of interest that the case of Hingst, in which the tumor was not removed, still had a post-operative life of five years with a palliative operation. One can readily see, however, that the radical operation has brought the best and most lasting results. The case of Körte, wherein complete cure has seemingly occurred, is a very encouraging example. Schofield has recently advocated implantation of radon to the carcinoma, doing the palliative cholecyst-enterostomy and implantation at one operation. This method may, in the future, supplant radical excision, but judging from the above table, one must acknowledge the fact that excision gives the best hope of five-year cure. With this analysis, moreover, we cannot help but feel that the operation of radical excision is certainly justifiable when compared to the possible six months of life to be obtained by the average palliative measures.

Methods and technic of operation were fully discussed by Cohen and Colp in 1927, and further literature has given us few improvements from this standpoint except as to preparation of the patients. Employment of calcium or sera to control abnormal bleeding and coagulation time so often occurring in these cases has been of some value. The intravenous use of glucose to prevent post-operative liver shock and liver shock due to sudden decompression of the biliary system has also done much to decrease the operative risk in jaundiced patients. The lesson to be gained from the literature seems to be the value of further palliative procedure, such as cholecystogastrostomy and gastro-enterostomy when symptoms develop after the radical operation. It seems logical that cholecystogastrostomy combined with gastro-enterostomy, should, by widely diverting both bile and food from the site of possible recurrence, be the palliative measures of choice even to prophylaxis when earliest symptoms of recurrence present themselves.

To the above list of five-year cures we have the privilege of adding another. This patient was reported before the American Surgical Society in 1925 as a one-year cure. The clinical record in brief is as follows:

F. M., age fifty-two, admitted to the medical division May 6, 1924, complaining of itching, jaundice and weakness, of four months' duration. His stools were light yellow



in color and he suffered with occasional indigestion. He was studied the usual time in the medical ward, and the following findings were reported: A palpable gall-bladder and enlarged liver. A Van den Bergh test slightly delayed direct, with indirect of 2.45 units. This was repeated five days later and the direct responded promptly, the faeces showing some bile pigment in the meantime. The phenoltetrachlorophthalein liver function test showed severe damage in that 20 per cent. of the dye was still present at the end of one hour. The Wassermann reaction was negative. Bleeding time was three minutes and coagulation time eight minutes.

He was transferred to the B. Service of the Surgical Department May 19, 1924, the Van den Bergh reaction having reached 5 units in the meantime. He was operated upon on May 20, 1924, with the provisional diagnosis of carcinoma of the head of the pancreas or common duct stone. At operation, a carcinoma of the ampulla of Vater about 1 inch in diameter was found by duodenotomy after opening of the common duct failed to reveal stones. This growth was removed in entirety by the cautery, and in order to avoid stricture by occlusion, a rubber tube was sutured in the common duct



FIG. 1.—Periampullar carcinoma.

and allowed to hang 3 inches in the duodenum. Following this procedure convalescence was uneventful except for breaking down of the wound necessitating resuture eight days after operation. An X-ray taken on day of discharge revealed the rubber tube still in place. Sections of the tumor showed typical cylindrical cell adenocarcinoma (Fig. 1).

The patient returned seven months later, symptom-free. X-ray examination showed no rubber tube present and the Van den Bergh reaction had been reduced to 1.4 units. One year later his Van den Bergh test had become normal; 0.5 unit and 0.2 unit when presented before the American Surgical Association, March 2, 1926.

In June of 1926, or more than two years after operation, he returned, complaining of indigestion, itching, with occasional jaundice and vomiting accompanied by chills and fever. He had lost 16 pounds in weight in the previous three months, but was able to continue with his work. A gastro-intestinal X-ray done at this time shows a compressed, elongated duodenal cap, probably from external pressure. Three weeks later his symptoms had cleared up considerably and his Van den Bergh was again recorded as 0.2 unit.

He was readmitted August 12, 1926, complaining of pain, chills, fever and severe

itching. He had clay-colored stools frequently but not continually, with bile in the urine. The Van den Bergh now was 3.5 units with an icteric index of 80. A cholecystoduodenostomy was done on August 17, 1926, from which he had a normal recovery with disappearance of all symptoms. At this operation the pancreas was found rather firm, but there were no definite signs of recurrence. A slight hernia developed in this wound, but he had remained perfectly well until January, 1927, when he commenced to suffer with pain and heaviness in the upper abdomen, gaseous eructation and nausea. These symptoms increased until he was readmitted on March 11, 1927, having suffered for ten days with severe, abdominal, cramp-like pains with vomiting. He had lost 18 pounds in the previous three months. A posterior gastro-enterostomy was done. The duodenum was found to be dilated but exploration was unsatisfactory because of the extensive and dense adhesions. No evidence of metastasis was present on superficial examination.

Following this operation, after a normal convalescence, the patient gained weight and for three months was entirely symptom-free. He then began to suffer with short attacks of epigastric pain, not related to meals. His stools were occasionally darkly colored. He was readmitted January 20, 1928, to the medical division, where studies revealed: Van den Bergh, delayed direct, indirect 1.4 units. Chest X-ray was negative for metastasis. The gastric analysis showed no free acid and the blood urea nitrogen was up to 34 milligrams per 100 cubic centimetres. A gastro-intestinal X-ray at this time showed a normally functioning gastro-enterostomy. The pylorus and duodenum did not fill and were therefore not observable. After being eight days on the medical service he was discharged, having improved greatly since admission; a slight tenderness being the only sign or symptom remaining.

Two months later he was readmitted to the surgical service, complaining of the same dull gnawing pain in the epigastrium, now coming on half an hour after eating and wearing away in the course of two hours. He could obtain no relief by diet or by alkalis, and an X-ray examination was therefore made at once. Melæna was now occasionally present, but bright red blood was never found in the stools. The gastro-intestinal X-ray made at this time showed a large duodenal cap and a well functioning gastro-enterostomy. Blood urea nitrogen was normal, 16 milligrams per 100 cubic centimetres, and the Van den Bergh showed 0.2 units. There was now a definite mass in the upper left epigastrium. This mass was tender and the size of an orange. The patient was given a treatment of intravenous lead, which was followed by deep X-ray therapy.

On the eleventh of September, 1928, he was readmitted, this time to the Neuro-surgical Service of Dr. Charles Frazier with the thought that chordotomy might give him relief of pain. At this time he was suffering extreme pain which doubled him up every attack, lasting two hours. Nothing relieved it except narcotics, which served to deaden it momentarily.

Physical examination revealed multiple masses of various size easily palpated through thin and emaciated abdominal walls. These masses varied in consistency, some being soft and others hard, filling the entire upper abdomen. Peristalsis was vigorous, painful and visible. The patient was very weak, his blood had become anæmic; hæmoglobin 40 per cent., red blood cells 3,500,000; but his Van den Bergh was still normal, 0.2 unit. Gastro-intestinal X-ray now showed a large pressure defect on the stomach due to the intestinal mass adjacent. It was obvious that the carcinoma was now rapidly spreading and metastasizing. Following several days' observation it was felt that chordotomy would not be advisable and the patient was discharged with narcotics to control his pain. He died January 27, 1929, or four years and eight months after operation. Post-mortem examination was not granted, but a communication from the family doctor revealed that œdema of the lungs, perhaps due to pulmonary metastasis, was a contributory cause of death. Thus, despite the need of three operative procedures, the patient lived some four years with comparative comfort, being able to

keep at his work all this time, and pain was acute only during the last four months of his life.

Following this case step by step through his post-operative life, one cannot help but feel that the radical operation for this disease is much to be justified, especially when aided by later palliative measures, and the case has been reviewed in detail for this purpose.

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## TORSION OF THE GREAT OMENTUM\*

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TORSION of the great omentum was first referred to in the literature by Pierre de Marchettis in 1851. We owe the first full description of the clinical picture and operative findings to Oberst who published an account of torsion of the omentum caused by an adhesive band to the right inguinal canal, in 1882. A similar case was reported by Bayer in 1898. The next account in the literature was by Hochenegg in 1900 whose report and treatise were very full.

Up to the present time there have been reported twenty-two cases of so-called "idiopathic" omental torsion, and 147 associated with inguinal hernia. This meagreness of reported cases is by no means indicative of the frequency of its occurrence. It is probable that many surgeons have encountered this pathology without reporting it. I am not discussing this subject because of the rarity of its occurrence but to urge its consideration in the differential diagnosis of the acute abdomen; especially in the male with pre-existing inguinal hernia and a leucocyte count too low for the clinical picture of acute appendicitis.

In the acute surgical abdomen a positive diagnosis is oftentimes admitted to be difficult and the list of possibilities is a long one. The differential diagnosis of Henock's purpura and intussusception, acute pancreatitis and enterospasm or organic intestinal obstruction, appendicitis and tuberculous peritonitis have only to be mentioned as examples of pitfalls into which the surgeon may stumble in his attempt to make an accurate pre-operative diagnosis.

Many acute surgical conditions of the abdomen present the same symptoms and signs in their earliest stages and this fact increases the difficulty of an accurate diagnosis.

Torsion of the omentum is not to be found mentioned in surgical text-books under the differential diagnosis of acute appendicitis or acute cholecystitis and few text-books mention it at all. Keen's *System of Surgery* mentions it. Thomson and Miles, sixth edition, gives a complete but short description of the disease.

Torsion of the omentum has usually been diagnosed acute cholecystitis or acute appendicitis. A pre-operative diagnosis of acute epiploitis may have been guessed but it has never been made with any degree of certainty, according to the literature.

Let us briefly consider the comparison of the clinical pictures of acute

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epiploitis due to torsion and acute appendicitis. Age is not a factor. Omental torsion has occurred between the ages of fourteen and sixty-three years.

| <i>Omental Torsion</i>                        | <i>Acute Appendicitis</i> |
|---|---------------------------|
| Sex .....Predominately male                   | Not so predominately male |
| Early pain ....Right iliac fossa 88 per cent. | Mid-abdominal more often  |
| Vomiting .....Infrequent                      | Common                    |
| Nausea .....Infrequent                        | Frequent                  |
| Pulse .....80-100                             | Rapid rising              |
| Temperature ..98°-100° F.                     | 99°-102° F.               |
| Rigidity .....Less marked                     | Early                     |
| Tumor .....Sudden and large                   | Slow development          |
| Percussion ....Dull                           | Resonant at first         |

The clinical picture presented by a patient suffering from an omental torsion will lead the experienced surgeon to operate at once, and this is only one of the many examples of how our treatment of acute abdominal disease has advanced beyond our powers of diagnosis.

Upon opening the abdomen in most of these cases previously reported, it was invariably noticed that the parietal peritoneum was cedematous and that upon opening the peritoneum there was a gush of sero-sanguinous fluid. This finding would be of some value to the operator where the incision was a McBurney, although we must remember that torsion of other viscera may cause sero-sanguinous peritoneal fluid.

The histology of the affected omentum in these cases reveals a venous thrombosis and a perivascular infiltration of mononuclear leucocytes, lymphocytes, and an occasional polymorphonuclear leucocyte. In no case have bacteria been found.

Omental torsion has been grouped under three distinct classes. The first class is the abdominal type where no hernia exists and there is no apparent cause for the torsion. The second class is the hernial type where a piece of twisted omentum lies in the hernial sac above, is associated with other viscera, or where the omental tip is connected to the inguinal canal by an adhesive band. The third class is that type secondary to other intra-abdominal pathology, most often appendicitis, where the right lower portion of the omentum is not in contact with the diseased appendix yet it is tersed on its pedicle and is gangrenous.

Cases have been reported in which a portion of the omentum was twisted on a pedicle from one to nine turns, also cases in which the entire great omentum was tersed on a pedicle.

There are many theories advanced as to the etiology of torsion of the omentum. The most plausible of these theories are:

1. Adhesions of the tip of the omentum causing the omentum to swing and twist a pedicle for itself as would a triangularly folded handkerchief when held between two hands and swung.

2. Exaggeration of normal movements such as a sudden strain, twist of the body or a jump. This theory is the most plausible one because in

## TORSION OF THE GREAT OMENTUM

most reported cases there is neither a contributing anatomic cause nor a history of trauma, while in a few reported cases, and one of my own, a history of sudden straining and twisting of the body was followed by pain.

3. Increased intestinal peristalsis is thought by some to cause omental twisting.

4. Some believe the anatomical arrangement of the blood vessels predisposes to torsion.

5. Others believe that a previous inflammatory process leaving a localized area of omental thickening is the cause of the twisting. The explanation being that the thickened portion would be more cumbersome in its movements than would be the normal portions.

These explanations are all, however, only theoretical. The accurate answer as to the true etiology may be either one, a combination, or something entirely different.

There is not a single case on record of omental torsion due to an adhesive band in a femoral hernial sac.

The operative mortality on all reported cases since 1882 has been about 5 per cent. Of these seven deaths five were due to post-operative pneumonia and two were due to peritonitis.

In conclusion let me repeat that omental torsion is not a rarity among intra-abdominal lesions. It has probably been encountered a number of times by most surgeons and the surgical treatment is very satisfactory. It would be diagnosed more frequently if considered in the differentiation of acute abdominal conditions.

Four cases of omental torsion are herewith reported. Two of these cases belong to the abdominal or so-called idiopathic type, of which one was operated upon the clinical diagnosis of acute cholecystitis and the other for acute appendicitis. Of the other two cases, one belongs to the type associated with inguinal hernia while the last one belongs to the type associated with other intra-abdominal pathology, in this case an acute appendicitis. Each of these four cases is a typical representative of its type.

CASE I.—C. C., male, aged forty-seven, was admitted to the Lankenau Hospital. His chief complaint was abdominal pain of forty-eight hours' duration. Prior to the onset of the pain, which was gradual, he had been perfectly well. There had been no vomiting. He was sent to the hospital with the diagnosis of acute appendicitis. On admission the temperature, pulse, and respirations were 98.6° F., 80 and 20 respectively. The abdomen was moderately distended and there was some rigidity of the lower right rectus. The pain was exaggerated upon coughing and on deep inspiration. The blood count showed a leucocytosis of 11,600 with a normal differential count. The diagnosis of acute appendicitis made by the referring physicians was concurred in.

At operation a segment of omentum practically gangrenous was located just to the right of the umbilicus; the mass was twisted three times upon itself and adherent to the anterior parietal peritoneum. The affected portion of the omentum was excised. A normal appendix was removed coincidentally. The abdomen was closed without

drainage and the patient was discharged on the tenth post-operative day after an uneventful convalescence.

CASE II.—F. S., male, aged thirty-three was admitted to the Lankenau Hospital. His chief complaint was pain in the right upper abdomen of two days' duration. The pain appeared suddenly and did not radiate. There was slight abatement after belching large amounts of gas but the pain returned more severely than previously. His physician sent him into the hospital diagnosed acute cholecystitis. On admission the temperature, pulse, and respiration were 98.2° F., 102, and 18 respectively. He was obese. The abdomen revealed marked tenderness over the gall-bladder area and pain occurred there upon pressing any part of the abdomen. No tenderness over McBurney's point. The blood count showed a white cell count of 7,600 with 75 per cent. polymorphonuclears. The icteric index was 6 while the van den Bergh was normal. The diagnosis of acute cholecystitis was concurred in. At operation a piece of slaty blue gangrenous omentum about the size of a silver dollar was found twisted twice on its pedicle just below the hepatic flexure of the colon. Gall-bladder and appendix were normal. The affected piece of omentum was excised. Abdomen closed without drainage and the patient discharged on the twelfth post-operative day after a normal convalescence.

CASE III.—C. D., male, age thirty-seven, was admitted to the Lankenau Hospital. His chief complaint was lower right abdominal pain of seven days' duration. The pain was diffuse at first and the onset was gradual. No nausea or vomiting. Has had a right inguinal hernia for eighteen years and a truss would not retain the rupture. His family physician was called in, diagnosed acute appendicitis, and ordered him to the hospital at once. On admission the temperature, pulse, and respiration were 100° F., 104, and 24 respectively. The abdomen was obese and full. Peristalsis was tinkling in character. In the right lower quadrant a very tender mass could be palpated. There was moderate lower right rectus rigidity. A hernial sac could be palpated on the right side as the patient coughed. There was a leucocytosis of 11,900 with a normal differential. The pre-operative diagnosis in this case was appendiceal abscess and right inguinal hernia.

At operation the right lower tip of the omentum was hæmorrhagic and gangrenous, forming the mass in the right lower abdomen. The distal tip of omentum was twisted into a narrow strand extending down into the right hernial sac. The omentum was excised well above the affected area. A normal appendix was removed coincidentally. The abdomen was closed to a cigarette drain in the pelvis. Drainage was out on the seventh day and the patient discharged on the eleventh day.

CASE IV.—H. T., male, age twenty-three, admitted to the Lankenau Hospital. His chief complaint was right lower abdominal pain of two days' duration and of gradual onset. He was somewhat nauseated but did not vomit. His physician was called in, diagnosed acute appendicitis and sent him to the hospital at once. On admission the temperature, pulse, and respiration were 98.4° F., 120, and 24 respectively. The examination of the abdomen revealed pain, tenderness, and rigidity in the right lower quadrant. No herniæ. The blood count showed a leucocytosis of 16,200 with 67 per cent. polymorphonuclears, 25 per cent. lymphocytes, and 8 large monocytes. The referring physician's diagnosis of acute appendicitis was concurred in.

At operation a very mildly inflamed subcæcal appendix was removed. A piece of strangulated, gangrenous omentum, twisted on its pedicle twice, was removed. This affected omentum was about four inches away from the appendix. The abdominal wall was closed without drainage and the patient was discharged in nine days.

In each of these cases upon opening the peritoneum, sero-sanguinous peritoneal fluid was encountered and in the last three cases there was localized œdema of the parietal peritoneum.

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# CARBUNCLE OF THE KIDNEY\*

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CARBUNCLE of the kidney constitutes a rare but definite lesion. Macroscopically, it closely resembles the similarly designated infection so commonly encountered in the cutaneous and subcutaneous tela of the body. The condition was first described by Israel in 1891. This clinical entity offers a good prognosis, if the diagnosis is made early and the operation timely, for the infection in its initial stage consists of a circumscribed zone of multiple suppurative foci.

A review of the literature disclosed a total of 58 available cases: J. Israel<sup>1</sup>, 1; Federoff, 1; Stucky, 1; W. Israel, 2; V. Herezel, 2; Ekehorn, 1; Kretschmer<sup>2</sup>, 2; Barth, 4; Aschner<sup>3</sup>, 4; Mathe, 1; Rescke<sup>4</sup>, 4; McWilliams, 1; Horn, 1; Colmers, 2; Furniss, 1; Fischer, 1; Eisendrath, 1; Zinn, 1; Rjasanzewa, 2; Smirnow<sup>5</sup>, 5; Klumow<sup>6</sup>, 1; Voss, 2; Meso, 1; Rothbart, 1; Lipshutz, 2; Shapiro<sup>7</sup>, 1; Thompson<sup>8</sup>, 1; Dick<sup>9</sup>, 3; Kohler, 3; Moore, 2; Lazarus, 2.

It is very probable that the chronic carbuncle is more common than is generally believed.

CASE I.—J. P. (No. 46355), male, married, aged thirty-four. Referred by Dr. A. I. Rubenstone. Admitted to Mt. Sinai Hospital, November 18, 1927. The patient noted that he had been below par in his general health for three months prior to his admission to the hospital. He began to complain of a dull, aching pain over the right loin on September 31, 1927. The pain did not radiate, although one attack of pain was apparently colicky in character. No spontaneous pain was present when he entered the hospital. Urinary symptoms were absent.

The patient was a rather poorly nourished, somewhat anæmic male adult. The heart and pulmonary system were negative. Nose and throat examination disclosed an acute sinusitis, diseased tonsils and deflected septum. The physical examination was essentially negative, with the exception of a slight increase in muscle resistance and moderate tenderness over the right loin.

*Blood Examination.*—On admission—11,000 leucocytes; 81 per cent polynuclears; hæmoglobin-60 per cent.; 4,000,000 red blood cells. Within a week of his entrance to the hospital, his total leucocyte count began to mount, varying from 18 to 23,000 white cells associated with an increase in polynuclears (85 to 93 per cent.). The increase in the leucocytosis and in the polynuclears was apparently the result of an invasion of the infection into the loose pararenal tissues. Additionally, there was a progressive secondary anæmia. Three weeks after admission his blood count was 55 per cent. hæmoglobin and 3,000,000 red blood cells. The urine was frequently totally negative, but at intervals a few leucocytes and a trace of albumin were noted.

Blood cultures repeatedly negative. Smears and cultures from the urine negative. Wassermann negative. X-ray of the kidneys negative for stone. X-ray of the chest was negative. Fluoroscopy, however, showed a slight diminution in the movements of the medial segment of the right half of the diaphragm during respiration.

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\*Read before the Philadelphia Academy of Surgery, December 1, 1930.

The temperature ranged from 99.5 to 103° F. At cystoscopy:—the bladder and ureteral orifices were normal and catheters passed readily up both ureters. Following the intravenous injection of 10 cubic centimetre of 0.5 per cent. indigocarmine, the latter appeared at the left ureteral orifice in 3½ minutes; its appearance at the right orifice was delayed for 30 minutes, indicating considerable dysfunction of the right kidney.

All of the positive clinical findings pointed to an infection of the right kidney, with a possible involvement of the pararenal tissues. A transfusion of 500 cubic centimetres was given to the patient in preparation for operation.

*Operation.*—Right lumbar nephrectomy (nitrous oxide and oxygen anaesthesia). The kidney was bound down by massive adhesions, the result of a perinephritis and the fibrous transformation of the perinephric fat. The upper half of the kidney was the site of a large carbuncle which had perforated into the perinephric space, producing additionally a perinephric abscess. The kidney, its thickened capsule, and fibrous perinephric fat were completely extirpated.

*Specimen.*—Right kidney. The kidney is larger than normal. The capsule was greatly thickened, measuring, in some places, 3 millimetres and was inseparably fused to the fibrous pararenal fat. The upper half of the kidney showed a distinct mass which was bulging, and numerous small areas yellow in color, which exuded a greenish-yellow pus. The cut surface of the kidney presented a speckled appearance and numerous petechiæ. Surrounding the large suppurating focus was a number of small nodes, the size of millet seeds, of the same character, but not directly connected with the large suppurative focus. The rest of the kidney exhibited evidence of a diffuse hyperæmia and cloudy swelling.

*Microscopic.*—The interstitial tissue between the tubules is densely infiltrated with polynuclear leucocytes. In some places the exudate has completely replaced the structure of the kidney. The glomeruli are not affected. The blood vessels are filled with thrombi. There is much fibrous tissue indicating the chronicity of the pathology.

*Diagnosis.*—Carbuncle of the kidney.

*Pus from Kidney.*—No tubercle bacillus found. Many gram-positive cocci. Culture showed staphylococcus aureus as did the guinea-pig inoculation.

*Convalescence.*—Convalescence was rather tardy, but marked by steady improvement. Discharged January 31, 1928. He has now completely recovered his health, assumed his normal activities, and has taken on 35 pounds in weight. Urine is now negative.

*Comments.*—The individuals affected are usually between the ages of twenty-two and fifty-five, although Barth<sup>10</sup> and Colmer each report one in a girl of ten, and Smirnow one in a girl aged fourteen. The primary focus in most of the cases is some staphylococcic infection of the skin, most commonly a carbuncle or hard furuncle. Such infections are pararitium, mastitis, osteomyelitis of the finger, angina, and in three of Smirnow's cases, influenza, have been tagged as the primary focus. It is a matter of common knowledge that patients with boils, carbuncles, and acute osteomyelitis, occasionally develop metastatic renal and pararenal infections with the staphylococcus, which is the causative agent of the primary infection. Cabot<sup>11</sup> has recently directed attention to the association of upper respiratory infections and infections of the kidney. The interval between the healing of the primary skin infection and the appearance of clinical evidence of a renal or pararenal infection, is variable, ranging from two weeks to seven months with an average interim of three to five weeks. In one of the included case reports,

three weeks intervened between the healing of a small furuncle of the buttock, which was self-treated and the development of clinical signs of a renal infection. In a number of the reported cases, trauma was noted as a definite cause. In some of the cases no primary focus could be elicited or demonstrated. Chiralla,<sup>13</sup> in a study of perinephric abscesses, noted that in two-thirds of the cases etiologic factors could not be found. It is probable, however, that the portal of entry of the infection was so trivial as to be overlooked or forgotten.

*Pathology.*—The infection begins in the interstitial portion of the cortex of the kidney and is practically always of hæmatogenous origin. Stoerck includes this type of infection under the general heading of "embolic suppurative nephritis."

From a pathologic viewpoint the first change produced in the kidney by the infected emboli is an infarct, which is soon converted into a suppurative focus. The base of this pyramidal-shaped infarct is always directed toward the cortex of the kidney, and the apex toward the pelvis. If only the small vessels are blocked, a renal abscess results; if many small vessels are occluded, multiple abscesses form and the entire viscus may be so affected. If the bacteria reaches the glomerular vessels, microscopic abscesses about glomeruli are produced (nephritis apostematosa). When a large vessel is blocked, either by bacteria or infected emboli, a renal carbuncle results. The apex of the pyramidal-shaped infarct is the site of the blocked vessel, and base of the pyramid is always directed toward the cortex. The destructive type, designated as renal carbuncle, is of rare occurrence as compared in frequency to the other types of renal abscess. In its original stage the infection is limited to the cortex, and in the overwhelming majority of cases, it is produced by one of the pus-producing cocci; staphylococcus aureus, and staphylococcus albus will be found in large numbers. The experimental production of infections of the urinary tract by intravenous injections of bacteria in the absence of obstruction to the urinary tract, gives a low percentage of positive results. The staphylococcus tends particularly to cause embolism of the vessels supplying the cortex, while the colon bacillus affects the vessels supplying the papillæ. It is difficult to explain why, in coliform lesions, the vessels of the papillæ are more liable to embolism than those supplying the cortex.

Considering the type of circulation of the kidney the latter must often be the site of both pyemic localization and innocent emboli. The infection, in a mild form, is probably more common than we believe, most of the cases terminating in spontaneous recovery. Cabot<sup>12</sup> in his comments on the cortical type of renal infection states: "My own experience has led me to believe that this type of coccus infection constituted a large majority of the cases, and that the opinion held some years, that in most of these cases severe destruction of the kidney occurred, which was likely to require operation, is probably wrong. With enlarging experience, I have found that the acute destructive type seems to constitute only a minority of the cases, and I believe that these lesions

when not too extensive, show a tendency to spontaneous recovery. In the kidneys here examined, the attempt at spontaneous recovery is clearly evident from the presence of large amounts of fibrous tissue." Essentially, the microscopic image is one of extensive perivascular infiltration, thrombotic vessels and the presence of a large amount of fibrous tissue. The kidney in the advanced destructive stage presents a speckled appearance, the result of the conglomeration of variously sized, small abscesses filled with thick pus, the individual abscesses being separated one from another by densely infiltrated renal parenchyma. The division between the carbuncle and the rest of the kidney is more or less sharply demarcated. In most of the cases the development of epi- para- or perinephritis is the immediate cause for the development of severe symptoms.

*Symptoms.*—Since the infection is largely confined to the interstitial portion of the kidney, and usually does not involve the conducting system, these cases frequently present a puzzling clinical picture. Most commonly, it masquerades under the clinical syndrome of a perinephric abscess and rarely, as a subphrenic abscess. Instances where the renal carbuncle has perforated into the loose pararenal tissue, thus producing additionally a perinephric infection, are not infrequent. Cases of this type are reported by Smirnow, Barth, Voos, Zinn, Furniss, Fischer, Eisendrath<sup>14</sup> and in the writer's case.

The symptoms are those of a mild or severe septicæmia with a swinging or continuous type of temperature elevation. Pains occur early and in the initial stage may be slight, and at times completely absent. Later in the disease, pain is constant, and varies in its intensity from a dull ache to a sharp localized pain.

More commonly the pain does not radiate, but in a number of the reported cases, the radiation of the pain to the abdomen was a prominent symptom. (Voos, Kretschmer, Mezo Bela, Smirnow.) The intimate anatomical relation of the ventral surface of the kidney to the peritoneum, duodenum, cæcum, colon, etc., readily accounts for the occurrence of abdominal pain, vomiting and meteorism in renal and pararenal infections. It is the anteriorly located cortical abscesses that are associated with symptoms that simulate appendicitis, cholecystitis and gastroenteritis. Such an abscess may perforate into the peritoneum and produce fatal peritonitis.

CASE II.—A massively obese female, aged thirty-six, was admitted to the hospital with a diagnosis of acute appendicitis. Temperature on admission was 100 degrees F., pulse rate 90, the leucocyte count was 19,000 with 88 per cent. of polynuclears. The previous history as far as could be obtained was negative. The examination of the urine showed only an occasional white cell, otherwise the findings were normal.

Careful physical examination disclosed marked tenderness over the right iliac fossa. The marked obesity rendered the examination for increased muscle tone or the presence or absence of the abdominal reflexes extremely unsatisfactory. No tenderness could be elicited over the loin, and in the angle between the twelfth rib and the erector spinæ mass. The clinical findings seemingly concurred with the diagnosis of acute appendicitis and the patient subjected to operation. The abdomen was opened through a right rectus incision. The peritoneal coat of intestines was injected.

the abdominal cavity contained considerable seropurulent exudate. What seemed a moderately inflamed appendix was removed. Exploration of the other viscera in the abdominal cavity showed no additional pathology. The kidneys could not be palpated because of the large amount of adipose tissue.

On the third post-operative day the patient developed severe ileus and other evidence of peritonitis; she died within two days in spite of the usual post-operative measures. The autopsy revealed a large cortical abscess of the carbuncular type which had ruptured into the peritoneal cavity producing a fatal peritonitis.

This case clearly shows the difficulty of diagnosing this lesion and how closely the anteriorly located abscess may mimic an acute abdominal lesion. The presence of severe pain points to the sequential development of a perinephric abscess. Tenderness is most acute in the region between the twelfth rib and muscles of the loin. Frequently, however, the local signs are indefinite. In the included cases nothing more than mild, deep tenderness and a little rigidity of the overlying muscles were clinically evident. Cough, movement and deep breathing may aggravate the pain. Careful examination also reveals some restriction of the respiratory movements of the affected side. In a number of the reported cases an ill-defined, extremely tender swelling was felt in the loin, and in a few instances an actual bulge was visible.

Urinary symptoms are at times absent, but frequency and dysuria and particularly nocturia have been reported. Complete urologic study is required for the diagnosis in the doubtful case. In six of the twenty-one cases collected by Voos<sup>15</sup> the urine is reported as normal. But a study of a centrifugalized specimen may show some red and white blood cells. In the fifteen remaining cases, some pathologic elements in the urine were found present. The most common urinary finding is a trace of albumin, a few red cells and some leucocytes. Study of the microscopic slides of the extirpated kidneys would seem to indicate that in very early stages of infection, the urine should exhibit a considerable number of leucocytes and bacteria, which later disappear, the result of the intensive fibrous tissue defense. In tracing the history of one of the included cases, the above statement is confirmed. In the advanced destructive stage, because of the large amount of fibrous tissue, the urinary findings are insignificant. An accurate estimation of pus in the urine by enumerating the formed elements of the blood (red blood corpuscles, leucocytes and casts) is best carried out in a counting chamber by a method similar in principle to that employed for blood counts.

Frankly, purulent urine clearly indicates that the infection has invaded the conduction system and was noted as present in only two of the collected cases (W. Israel and Mezo Bala).<sup>16</sup> Bacteriologic study of the urine may reveal staphylococci.

*Diagnosis.*—The recognition of this malady in most of the reported cases was made only at operation. Yet a careful clinical survey and a complete urologic study should lead to the diagnosis.

Clinically, carbuncle of the kidney not infrequently pursues a chronic insidious course, and Beer<sup>21</sup> very aptly labels this lesion with the caption, "silent infection of the kidney." The presence of a pyrexial illness, with or

without rigors, pain, and tenderness over the loin, a persistent leucocytosis plus insignificant urinary findings, or even a normal urine, constitute the main signs and symptoms upon which the diagnosis is based. If, added to the latter, there is a history of a recent staphylococcic infection, or influenza and more or less impairment in the function of the infected kidney, the clinical picture is complete. Rothbart in one case established the diagnosis by means of the X-ray, noting the formation of an increasing shadow about the kidney upon repeated röntgenograms. Beer notes that in cases of cortical abscess in which the symptoms have subsided and diagnosis was difficult, activation of the focus by injecting staphylococcus aureus vaccine in a dose of from 100 million to 500 million, acts as a provocative test and accentuates the clinical manifestations.

Acute diffuse suppurative infection of the kidney may be impossible of differentiation from carbuncle of the kidney, the former, however, begins acutely and runs a more acute course.

The acute diffuse embolic type of renal infection has been well studied by George Emerson Brewer.<sup>22</sup> Brewer's early interest in this subject was awakened by four or five examples of the severe or fulminating type of this disease, all of which proved fatal. Three autopsies demonstrated that the disease was unilateral and consisted of multiple embolic suppurative lesions, which in the observed cases, resulted in complete destruction of the kidney and an overwhelming and fatal toxæmia. As a result of this experience, a series of animal experiments were carried out. Sixteen animals were given an intravenous injection of pathogenic bacteria, and in addition to the inoculation, received an injury to one kidney. Five showed no lesion or only hyperæmia and parenchymatous degeneration. Two of the animals died within twenty-four hours of acute septic intoxication; of the remaining eleven, all developed surgical lesions of the kidney. The microscopy of the lesion was identical with that found in acute hæmatogenous renal infections, consisting of a plugging of the smaller arteries and capillary vessels with groups of organisms. Plugging of large vessels produced triangular septic infarcts. It was Brewer's opinion that the various types of renal hæmatogenous infections are but different stages of the same process. Brewer produced these lesions in animals by bacillus coli, streptococcus pyogenes, staphylococcus pyogenes aureus, bacillus typhosus and the pyocyaneus. The acute fulminating type of infection is well exemplified in the following case:

CASE III.—(No. 46793.) M. D., female, aged fifty-four, referred by Dr. Frank Leivy. Patient was admitted January 9, 1928, for the purpose of reducing her high blood pressure (220-210) which was of four years' duration. Incidentally, she complained of pain over the loin and painful urination. The patient, a rather obese female, complained of dyspnœa, severe substernal distress, and showed symptoms of cardiac decompensation.

X-ray of the lungs showed extensive peribronchial and alveolar infiltration with calcific deposits throughout. A large mass, four inches in diameter, was observed in the mediastinum involving chiefly the right side. The heart is displaced to the right, but appears normal. The right half of the diaphragm is smooth and rounder than

normal, the dome of the left half is excessively high, being two and one-half inches above the right. The left diaphragm under the fluoroscope appeared definitely fixed. There was no evidence of pleurisy or effusion. The mass noted in the mediastinum was suggestive of a sarcoma. X-ray of the kidneys disclosed no abnormalities.

Blood count on admission was 8700 white blood cells. Repeated blood counts later showed a persistent leucocytosis, 17,000 to 29,000. Urine at all times showed pus, red blood cells but no casts. Blood chemistry 26 milligrams of urea, 115 milligrams blood sugar. Blood Wassermann was negative. Mosenthal test 11.19, NaCl 0.07 per cent. carbon dioxide 47 volume per cent. per 100 cubic centimetres of blood. Cultures from the kidneys disclosed bacillus coli with gram-negative and gram-positive bacilli. Blood cultures negative.

The urologic study showed bladder and ureteral orifices normal; indigo-carmin eliminated by both kidneys in nine minutes. Pycelograph disclosed a suspicious defect in the left kidney pelvis. A severe reaction followed the pycelography. Temperature rising to 103, pulse 110, associated with an increase in the severity of the pain over the left loin. The following day the patient had a chill lasting over five minutes, which was followed by unconsciousness for ten minutes. Pulse became thready and rapid, rising to 104. Blood pressure 160, heart action was very feeble. The patient continued to be stuporous, complaining of weakness and left lumbar pain. The case appeared as one of cardiac collapse with failure of renal function. Tenderness over the left renal region was marked. A catheterized specimen of urine now showed frank blood and many leucocytes. The pyrexial reaction was probably due to the lighting up of a latent infection in the left kidney. Cystoscopy was performed February 10, 1928. A No. 5 catheter was placed in the left ureter for drainage, from which catheter bloody urine appeared. The patient failed to improve, vomiting appeared and abdominal distention manifested itself. The catheter was removed at the end of two days, but the pain and tenderness over the left kidney persisted. Examination at this time showed increased resistance and tenderness over the left loin, the diaphragm moved freely. In view of the persistence of the pain and moderate tenderness over the left loin, an exploration of the kidney and perirenal space under local anæsthesia, was determined.

Operation February 15, 1928. Left lumbar nephrectomy (paravertebral and abdominal field block anæsthesia). The left kidney was found greatly enlarged, swollen and œdematous and was removed.

Convalescence from the operation was markedly smooth, showing a steady improvement in general symptoms, and a gradual and complete clearing up of the septic state.

The patient was discharged March 18, 1928, with the wound almost healed, her general condition much improved. The mass noted in the mediastinum was still present and showed no change in size. Her blood pressure is now 140 and shows no signs of elevation. The patient has resumed her household duties and is enjoying a fair state of health.

*Pathologic Examination.*—The kidney was considerably larger than normal, measuring  $15 \times 9\frac{1}{2}$  centimetres and weighing 315 grams. The surface of the kidney was roughly granular, presenting numerous millet-sized seed nodes, many of which were aggregated in groups. Some of the nodes were dark red, others yellowish in color. The cut surface of the kidney was distinctly swollen and the cortex irregular. The pyramids were dark red and bulging. The mucosa of the pelvis and calices were hyperæmic and swollen. Many microscopic sections were made of every part of the kidney, disclosing a diffuse renal infection. Some portions near the cortex presented a complete loss of the normal renal picture—remnants of necrotic tubules and glomeruli, and a dense leucocytic infiltration. The kidney exhibited a massive and dense accumulation and diffusion of leucocytes, both polynuclears and lymphocytes. The tubules, with the exception of an occasional necrotic area, revealed only a high degree of cloudy swelling. The glomeruli were distinctly hyperæmic, and in certain areas a serous exudate filled the space of Bowman. The perivascular spaces between the

glomeruli were particularly affected, the leucocytic infiltration spread radiating from the perivascular spaces. The picture is that of an acute diffuse suppurative nephritis. Some of the glomeruli are hyalinated and the walls of the blood vessels present evidence of arteriosclerosis.

*Diagnosis.*—Acute diffuse suppurative nephritis (early stage). Arteriosclerotic kidney (slight stage).

*Bacteriologic Report.*—Culture of kidney (post-operative). Direct smear: Many pus cells, gram-negative bacilli, few gram culture: *B. coli*.

Radiation of the pain to the abdomen and the presence of a mass in the right iliac fossa may lead to a diagnosis of appendiceal abscess. Such a case is reported by Meso.<sup>16</sup>

The patient, a girl, aged eighteen, was admitted to the hospital with a diagnosis of an appendiceal abscess. A mass the size of a fist occupied the right iliac fossa. Catheterization of the right ureter revealed pus. The left kidney was normal. Upon these findings a diagnosis of appendiceal abscess was made with a resulting secondary pyelitis. At operation the appendix was found to be normal, but exposure of the right kidney revealed that its lower half was the seat of a large carbuncle. Because of the long duration of the illness, and the poor condition of the patient, only incision and drainage were performed. Recovery ensued.

*Treatment.*—Excellent results follow nephrectomy, provided the other kidney is normal. Toxic nephritis in the other kidney does not contra-indicate operation. Colmer's analysis of sixteen cases shows that two died without operation, and four cases in which only a nephrotomy was done, also died. The infection in the kidney at the time of operation is usually so far advanced that only removal of the affected viscus offers a promise of cure. Only three of the collected cases showed an involvement of both kidneys (Kretschmer, Stucky and Rjasanzewa). Stucky's case is of particular interest for it is the only available recorded instance in which a carbuncle developed in both kidneys with the recovery of the patient. In the latter patient, five weeks after the removal of one kidney, which was the site of carbuncle, the other kidney revealed clinical signs of a carbuncle. The latter was drained and the patient subsequently discharged as cured. Incision and drainage leaves a large infected area and exposes the patient to a possible hazard of a difficult secondary nephrectomy. In a number of instances, as noted above, the primary operation consisted of incision and drainage of a perinephric abscess. Recovery did not take place and a subsequent operation disclosed a carbuncle of the kidney as the cause of a perinephric abscess necessitating a nephrectomy.

Kohler has successfully treated two cases of solitary carbuncle of the kidney with the following technic. The kidney is exposed by means of a lumbar incision, delivered into the wound and decapsulated. The exposed kidney is now punctured in some twenty places by means of a small cannula, both infected and uninfected portions of the viscus being punctured. The site of each puncture is injected with 2 per cent. Rivanol. Most of the injected antiseptic flows out through the puncture openings. The kidney is now replaced, the wound closed, a small gauze drain being introduced through the lower angle. It is well to recall that Brewer<sup>22</sup> advised decapsulation of the



kidney as the treatment of choice in the intermediate type of acute hæmatogenous renal infections, a group which has been aptly termed the glaucomatous kidney.

When the case is subjected to operation, while the infection is limited to a small area of the cortex, resection of the infected kidney focus may be feasible. The latter procedure was successfully carried out four times. The conservative resection of the infected focus, in properly selected cases based upon the premises of the pathology of this lesion, is a sound and logical operation since the infection begins in the cortex and is rather sharply demarcated from the uninvolved part of the kidney.

The infarct in the early stage of the infection can easily be removed and the resultant cavity packed with gauze. The wound should be left open to prevent an extensive area of infection.

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# TRANSACTIONS

OF THE

## PHILADELPHIA ACADEMY OF SURGERY

STATED MEETING HELD NOVEMBER 3, 1930

The Vice-president, DR. JOHN SPEESE, in the chair  
CALVIN M. SMYTH, JR., M.D., Recorder

### PRIMARY GIANT-CELL TUMOR OF THE PATELLA

DR. LEONARD G. DOBSON (by invitation) reported the case of a man aged twenty-four who was admitted in the orthopædic service of Dr. A. B. Gill in the Hospital of the University of Pennsylvania January 28, 1930 complaining of pain and swelling of the right knee. A year previous to admission he had fallen, striking his acutely flexed right knee on the pavement. He felt something snap in his knee and had severe pain when moving his leg. The knee was strapped but had remained swollen and tender ever since. For several months previous to admission he had noticed that the right knee cap was getting larger, was hot to the touch and that motion of the leg, especially extension, was painful. When admitted the right patella was enlarged, smooth and the skin over the patella was red and hot to the touch. Pressure upon the patella was very painful. Repeated studies of the blood and urine were negative for pathology and the blood Wassermann was negative in all antigens. Old tuberculin intracutaneously was negative for reaction for .1 milligram in twenty-four and forty-eight hours.

A röntgenogram of the knees taken January 13 showed that there had been an old fracture through the right patella. In addition there is now considerable rarefaction and some tendency to trabeculation of the patella. This appearance is rather unusual for a simple fracture of the patella.

At operation January 30, by Dr. A. Bruce Gill, the vessels about the patella were found congested. The patellar ligament was elevated subperiosteally and there was free bleeding from the congested veins. The cortex of the patella was firm but when a small piece of the cortex was removed the patella was found to be a shell filled with blood and dark material which resembled degenerated blood clots. The soft, spongy material was carefully curetted out. The interior of the patella bled very freely and was packed with gauze to control the hæmorrhage; the anterior portion of the cortex was crushed in and the wound closed, leaving the end of the gauze packing extending out of the wound. A posterior plaster splint was applied.

Culture of the material removed from the patella revealed no growth except a few diphtheroids. Dr. Herbert Fox reported on the microscopic examination of the tissue as follows: "Within a mass of blood was found a piece of tissue showing giant-cell tumor of bone, suggestive of sarcoma be-

cause of the irregularity and indefiniteness of the blood spaces. Examination of the decalcified bone from the cortex shows some rarefaction, fibrillary bone formation and masses of pigment, but no tumor was found."

Following the operation the patient made an uneventful recovery. The gauze packing was removed on the second day after the operation. The posterior splint was left on for six weeks after operation, being removed for dressings. Examination March 12 showed the patient able to walk but there was still some tenderness over the patella. X-Ray examination at that time showed: "Marked improvement in the right patella since last examination as indicated by considerable new bone formation. There is still some rarefaction."

Follow-up on the patient ten months after operation found him com-



FIG. 1.—Low power photomicrograph of the tumor tissue (x 250) showing chronic inflammation, bone spicules and giant cells.

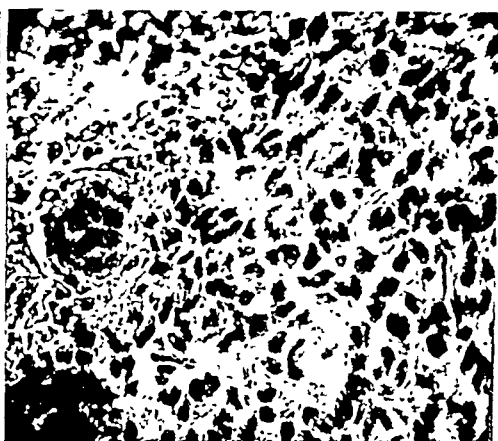


FIG. 2.—High-power photomicrograph (x 700) of the tumor tissue. Shows the very cellular cytoplasm.

pletely recovered and in excellent health. The right patella was no longer tender and was about the size of the left.

The reporter stated that tumors of the patella are very rare. Cole<sup>1</sup> in 1925 reported the first benign cyst of the patella. He surveyed the literature, both American and foreign, and found twenty-four other cases of primary tumor of the patella. These included all the common tumors of bone except myxoma. In these twenty-five cases were included three cases of giant-cell tumor of the patella. In 1924 Faltin<sup>2</sup> reported a case of giant-cell tumor of the patella which had not been included in the three reported by Cole. King and Towne<sup>3</sup> in 1929 reported the fifth case of giant-cell tumor of the patella. The case being reported is therefore the sixth case of primary giant-cell tumor of the patella recorded in the literature.

Giant-cell tumor is the term now generally used to designate a specific tumor. The condition has variously been called giant-cell sarcoma, myeloid sarcoma, hæmorrhagic osseous dystrophy, myeloma, osteitis fibrosa with giant cells and chronic hæmorrhagic osteomyelitis.

Lebert<sup>4</sup> is credited with first recognizing the condition in 1845. He noted

the giant cells in certain medullary tumors but did not at first separate the benign giant-cell tumor from malignant sarcoma of bone. Robin,<sup>5</sup> in 1850, described certain benign tumors of bone which contained many giant cells. Paget<sup>6</sup> further described the condition in 1853. In 1860 Nélaton<sup>7</sup> wrote a monograph on the subject describing the reddish, jelly-like appearance of the tumor tissue. He noted its capacity to absorb bone and widen the marrow cavity and fully established its benign course and the wisdom of conservative treatment. In 1879 Gross<sup>8</sup> presented the results of the study of seventy cases of giant-cell tumor and also emphasized their benign nature.

Although many writers had emphasized the benign nature of giant-cell tumors most of the surgeons treated the condition as malignant and employed radical treatment until Bloodgood<sup>9</sup> in 1910 again pointed out their benign nature. In 1920 Bloodgood<sup>9</sup> reported forty-seven cases of giant-cell tumor in none of which had metastasis occurred. Codman<sup>11</sup> in 1925 reported that 100 cases of giant-cell tumor had been registered without a true case of metastasis. Stone and Ewing<sup>10</sup> in 1922 held that rarely if ever does a true giant-cell tumor metastasize. Cole<sup>1</sup> in 1925 stated that giant-cell tumors are benign and could be cured by curettement followed by cauterization.

Authors do not share the opinion that all giant-cell tumors are benign. Coley<sup>12</sup> in 1924 presented an analysis of fifty cases of giant-cell tumor and found that metastasis had occurred in nine. In 1927<sup>13</sup> he reported follow-ups on fifty cases, included nineteen new cases and reached the conclusion that, "It is not always possible to differentiate the malignant from the benign cases by the clinical Röntgen-ray and microscopic data. Giant-cell sarcoma, or 'giant-cell tumor' as it is designated by most pathologists today while in the great majority of cases, a benign or at least only locally malignant lesion, should still be classed as a sarcoma since in certain cases it has all the clinical features of a malignant bone tumor causing death by metastases."

Chatterton and Flagstad<sup>14</sup> in 1927 reported two cases which had been diagnosed giant-cell tumor microscopically which developed malignant changes.

Single giant-cell tumors are not uncommon. The literature contains reports of several hundred cases. In 1927 Alexander and Crawford<sup>15</sup> reported a case of multiple giant-cell tumors and included a summary of twenty-four such cases collected from American and foreign literature.

Giant-cell tumors most often appear at the ends of the long bones, where, according to Christensen,<sup>16</sup> "there is an epiphyseal disc of maximal growth, where the growth period is longest and where the natural growth momentum is greatest." They also arise in the maxillæ (epulis type) and according to Ewing<sup>10</sup> very similar tumors occur in the capsules of joints and along the tendon sheaths and bursæ.

In the long bones giant-cell tumors produce reddish, jelly-like masses resembling granulation tissue and replacing the cancellous portions of the bone. The tumor may expand the shaft of the bone with the periosteum laying down an advancing shell of new bone. The shell of bone may be-

come so thin that it will crackle. The centre resembles splenic tissue except it has a firmer opaque cut surface and the central cystic areas are soft and infiltrated with blood. The outer bony shell may become thin and allow passage of the tumor tissue but there is seldom any tendency toward invasion of soft parts.

Giant-cell tumors are characterized by the abundance of large giant cells containing many small, separate oval nuclei. The tumors are believed to take origin from the fibrous tissue framework of bone, either from the periosteum or endosteum. The etiology of this type of tumor is obscure but it is quite well established that trauma is the most common cause of single lesions. The classification of giant-cell tumor is unsettled; some claiming it is inflammatory, others neoplastic, and still others that it is a mixture of the two. Alexander and Crawford<sup>15</sup> state that, "It is generally considered as resulting from some chronic irritation, which may follow a metabolic disorder." They further account for the development of the condition as follows: "The inflammatory proliferation of tissue is then essentially a regenerative process which has for its aim the compensation of the lesion produced by the cause of inflammation. Under special conditions this leads to a hyperplastic proliferation of connective tissue, frustrates its own aim and causes new damage. This is particularly the case when, as a result of the inflammation in the organism, there is kept up a permanent condition of inflammation. The bone tissue thus replaced by cellular tissue softens and produces multiple bone cysts lined with fibrous tissue and filled with clear fluid, fibrocystic osteitis, or within the fibrous tissue lining the giant-cell tumor develops."

*Giant-cell tumors grow slowly, do not metastasize, appear trabeculated by X-ray and do not produce cachexia.* The tumors may be present an indefinite time without giving rise to symptoms and often the occurrence of pathologic fractures is the first indication of their presence.

Diagnosis is based on the history, usually that of trauma; on the characteristic trabeculations by X-ray; and biopsy with microscopic examination.

The treatment generally advocated in cases of giant-cell tumor consists in thorough curettage with or without the application of pure carbolic acid followed by alcohol or with 20 per cent. zinc chloride. If the cavity is large it may be Dakinized, but usually simple packing is adequate. X-ray gives excellent results and numerous cures have been reported. Herendeen<sup>17</sup> in January, 1930, reported three cases of giant-cell tumor that had responded very well to X-ray therapy.

Regarding the rarity of tumors of the patella Christensen<sup>16</sup> states: "The patella seems singularly immune to bone tumors in spite of the fact that it is probably subjected to a far greater amount of trauma than any other bone in the body. It seems reasonable to assume that the immunity to bone tumors which the patella enjoys is probably due to the absence or loss of growth restraint, incident to active diaphyseal growth and pressure epiphyses. The fact that the patella develops from an endochondral center, that it has

## PHRENIC NERVE EXERESIS FOR LUNG ABSCESS

a relatively short period of growth, and that it is a sesamoid bone may be of importance."

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DR. A. BRUCE GILL remarked that out of twenty-seven cases reported in the literature this is only the sixth one of a primary growth in the patella. The report from the X-ray department suggested that it might be a giant-cell tumor, but the speaker could not entirely dismiss the thought that it might be a cyst and when he opened the cortex and found a very soft mass, which closely resembled an old blood clot, he thought he was dealing with a hæmorrhagic cyst; free bleeding also suggested that. The mass was so soft it was difficult to get out for microscopic examination.

## PHRENIC NERVE EXERESIS FOR LUNG ABSCESS

DR. RICHARD H. OVERHOLT (by invitation) presented a man aged twenty-five, who was admitted in the medical service of the Hospital of the University of Pennsylvania September 14, 1928. He had had a tonsillectomy under general anæsthesia four weeks previously, which was followed in a week's time by pain in the chest, cough, foul expectoration and fever. He had lost sixteen pounds in weight. There were no other symptoms.

Physical examination revealed nothing remarkable except an area in the right chest in the posterior axillary line over which the breath sounds were harsh and occasional râles could be heard. There was a moderate secondary anæmia, the hæmoglobin being 62 per cent. The leucocyte count was 15,400. The Wassermann reaction was negative. Acid-fast organisms were not

present in the sputum. A röntgenogram of the chest revealed an abscess in the lower portion of the right upper lobe, centrally located. Bronchoscopic examination showed mucopurulent material coming from the right upper main bronchus. A smear and culture of this material showed a mixed group of streptococci, staphylococci and micrococcus catarrhalis but no fusiform organisms or spirilla were observed.

Six bronchoscopic treatments were given over a period of four weeks at the end of which time the lesion had progressed in size and had extended to the periphery of the lung (Fig. 3). External drainage was recommended and the patient was transferred October 12, 1930, to the surgical service of Dr. George P. Muller.

An exeresis of the right phrenic nerve was done and this followed in three days by a first-stage thoracotomy by Dr. Selling Brill. A portion of the



FIG. 3.—Case J. B. Röntgenogram made six weeks after onset of symptoms of lung abscess. Lesion in lower portion of right upper lobe. Note size of lesion and extension to the periphery.



FIG. 4.—Case J. B. Röntgenogram made two weeks after right phrenic nerve evulsion and one week after first-stage thoracotomy. Three inches of the seventh and eighth ribs over the lesion had been removed and the wound packed with gauze. Note diminished size of right thorax due to elevated position of the diaphragm and almost complete disappearance of the lung abscess. Decision not to complete surgical drainage was made at this time.

eighth rib was excised in the posterior axillary line. In the course of the procedure the pleura was injured and an accidental pneumothorax resulted. The lung was immediately reexpanded by positive pressure anæsthesia and the rent in the pleura closed. A metal marker and gauze packing were placed in the wound. A subsequent röntgenogram showed the marker to be slightly below the abscess so that on October 20 (four days later) Doctor Muller enlarged the thoracotomy opening, resected the next rib above and repacked the wound. Immediately following these preliminary procedures, the patient's cough and expectoration subsided and the temperature dropped to normal. A röntgenogram of the chest October 27 (fourteen days after

## ELECTROCAUTERIZATION IN TREATMENT OF HUMAN BITES

phrenic exeresis and seven days after first-stage thoracotomy) showed an almost complete disappearance of the pulmonary lesion (Fig. 4). Because of the clinical and röntgenological improvement, the second-stage operation was not carried out so that actual surgical drainage of the abscess was not done. The patient was discharged two weeks after the last operation with a healed thoracic wound.

The patient was seen in the follow-up clinic one month later. All symptoms and signs of a pulmonary abscess had disappeared. He had been able to resume his former work. A röntgenogram gave evidence of slight fibrosis at the site of the previous lesion. The diaphragm on the right side was elevated and restricted in its movement (Fig. 3). After two years the patient was reëxamined. There had been no recurrence of the lesion and the röntgenogram showed a clear lung field on the right with a persisting diaphragmatic elevation.

The speaker remarked that the points of interest in this case are: (1) The rapid disappearance (two weeks' time) of a large pulmonary abscess during the course of surgical treatment without the necessity of actually draining the abscess; (2) the probable value of phrenic nerve interruption in the treatment of a thin-walled, easily collapsible, pulmonary abscess; and (3) the difficulty of evaluating the effect of the different surgical procedures in this case. The accidental pneumothorax was probably of little moment in that the lung was reëxpanded at the time and a röntgenogram forty-eight hours after operation did not show air in the pleural cavity. The removal of two ribs over the site of the abscess may have released the parietal pleura sufficiently to aid in the collapse of the walls of the abscess cavity which was so close to the periphery. Undoubtedly, most of the diminution in thoracic volume which permitted the walls of the abscess to collapse and obliterate the cavity was due to diaphragmatic relaxation. Because of the rapid disappearance of the pulmonary lesion in this case, the question is raised as to whether permanent diaphragmatic paralysis was necessary. Temporary paralysis by only crushing the nerve might have been sufficient.

## ELECTROCAUTERIZATION IN TREATMENT OF HUMAN BITES

DR. WILLIAM BATES read a paper with the above title, for which see page 641.

DR. HUBLEY R. OWEN said that in his work as a Police Surgeon he had had 200 cases of human bites in twenty-three years. In spite of the fact that he has tried every known treatment, he personally feels that he is not getting any better results now than twenty years ago. This same character of wound is received by more or less peaceful policemen making prisoners. Some years ago he reported two chancres developing from wounds of this character. He has not been able to get the same results as Doctor Bates with the cautery, but perhaps did not try it sufficiently. He has tried everything; one of the main things he has had to contend with is internes sewing these wounds up without drainage. He always opens the wounds widely under gas anæsthesia. Exposed metacarpo-phalangeal joints in these cases show rapid destruction



of the cartilage, probably because the impact is one of the cartilage originally and because of the poor blood supply. Infection and ankylosis of the metacarpo-phalangeal joint often occur. One case required amputation. The speaker asked Doctor Bates how far he suggested going with the cautery when tendons were exposed. Doctor Owen is at present treating these cases by wide incision under general anaesthesia followed by continuous immersion in warm boric solution. He will be glad to try electrocauterization again.

DR. JOHN FLICK said that he had been trying to study cases of human bites bacteriologically but unless examination is made very promptly and very carefully the spirochetes are missed; they are difficult to culture and unless the material removed is examined within a half hour the organisms are not found.

DR. M. J. HARKINS remarked that Doctor Bates' success with cauterization might be due to the fact that the severe course of many cases of bites is due to invasion by anaërobic bacteria. Many antiseptics have little if any value in this type of infection and it may be that the severe disinfection of the cauterization is responsible for the cleansing effect.

DR. WILLIAM BATES said that after going over his findings and various reports in the literature about the types of infection, he decided to wait for a few more cases and have them cultured before treating them, but none of these showed the streptococcus fusiformis. Regarding depth of cauterization, he thought one would be justified in carrying it to the point of complete débridement, even though it was necessary to sacrifice a tendon.

#### COMPARATIVE STUDIES OF ANTISEPTICS IN EXPERIMENTALLY PRODUCED LOCAL INFECTIONS

DRS. ELI SALEEBY and M. J. HARKINS, by invitation, read a paper with the above title.

#### END-RESULTS IN RADICAL OPERATIONS FOR CARCINOMA OF THE PERIAMPULLAR REGION

DR. GEORGE P. MULLER, and, by invitation, DR. LEE RADEMAKER read a paper with the above title, for which see page 755.

STATED MEETING HELD DECEMBER 1, 1930

The President, DR. GEORGE P. MULLER, in the Chair

CALVIN M. SMYTH, JR., M.D., Recorder

#### PERFORATED DIVERTICULITIS OF THE SIGMOID

DR. S. DANA WEEDEER reported the case of a man, age forty-one, who was admitted to Chestnut Hill Hospital in the service of Dr. William B. Swartley, November 30, 1929. His chief complaint was abdominal pain. Seven days prior to admission he was seized with a dull pain in the left lower abdomen following a meal. The pain was relieved by taking soda, but returned two days later and was not relieved by taking soda. The pain

continued until the day before admission when it became much more severe. He had a daily bowel movement until two days before admission, since which time he had been constipated and vomited frequently. There was no blood noticed at any time in his stools and no history of previous attacks of similar pain or other symptoms referable to the colon.

When admitted there was some distention of the abdomen with tenderness and some rigidity over the left lower quadrant. No masses could be palpated. The peristalsis was greatly diminished. Rectal examination revealed a tender mass in the left side. The rest of the physical examination was essentially negative. The temperature was 99, pulse 100, respirations 20. The X-ray report on a barium enema was as follows: "There is a delay in filling, apparently due to spasm of the colon. Coils of ascending colon are bent on themselves whether or not due to adhesions is impossible to say." The blood count showed hæmoglobin of 75 per cent., red blood cells, 3,800,000, white blood cells 15,000.

At operation on December 1, on opening the peritoneum a brownish fluid escaped. Further exploration revealed brownish purulent material with a faecal odor in the neighborhood of the sigmoid. Thick creamy pus escaped from deep in the pelvis. There were two faecal concretions free in the peritoneal cavity beside a hole in the sigmoid large enough to admit the tip of the little finger. The mesentery of the sigmoid was greatly thickened, oedematous, covered with fibrin and in several places necrotic. The perforation was closed and three cigarette drains and a rubber tube inserted. The patient died three days later.

DOCTOR WEEDEER reported a second case which also bears out the observation that diverticulitis occurs most commonly in middle-aged rather obese subjects, a man aged forty, admitted to the Germantown Hospital, November 29, 1928, in the service of Dr. Edward B. Hodge. His chief complaint was pain in the left lower abdomen. The pain began the day before admission to the hospital for which he took Epsom salts which purged him freely. There was no nausea or vomiting. For some years he had taken milk of magnesia for indigestion and constipation. The man did not look acutely ill. There was tenderness and slight rigidity in the left lower abdomen, the point of greatest tenderness being about an inch and a half from the umbilicus on a line drawn from the umbilicus to the anterior superior spine of the ilium. Rectal examination revealed a tender mass slightly to the left of the mid-line. The examination was otherwise negative except for a systolic murmur heard at the apex of the heart. The temperature was 99.6, pulse 100, respiration 24. The white blood cell count was 12,500; blood Wassermann, negative.

At operation November 29, a search was made for Meckel's diverticulum but none was found. The gall-bladder was normal; no masses were found in the liver; the stomach, duodenum and the appendix were normal. A mass, hard and indurated, was found in the pelvis which proved to be contained within the sigmoid. There was considerable oedema of the mesentery and epiploic appendages, several of which were attached by fibrinous exudate over the inner aspect of the sigmoid. By separating the peritoneum lateral to the sigmoid, with its mass, it was possible to deliver this loop of sigmoid through a second incision in the left lower quadrant, the Mikulicz procedure having been determined upon. A glass rod was run through the mesentery of the loop in order to hold it. The mid-line incision was then closed.

The second stage was done on December 6, the loop of sigmoid being removed by the cautery. Two days later a clamp was applied to obliterate

the spur. The clamp came off on the twelfth day. As there was not sufficient spur destroyed the clamp was reapplied and it finally cut through by the end of the fourth week and the final stage was done January 3, 1929.

On January 17, emphysema was noticed extending over the left lower abdomen and scrotum. There was an elevation of temperature to 101 and pulse to 100. However, the patient did not appear to be toxic. The wound was opened down to the aponeurosis and a brownish foul-smelling, purulent material and gas were liberated. In twenty-four hours the emphysema had extended to the left ankle; but the temperature had subsided and the pulse fell to 80. By January 31 the emphysema had practically disappeared and the wound looked healthy. An anaërobic culture was made to determine the presence of Welch's bacillus which was not found. The culture showed bacillus coli communis, a member of the dysenterial group and bacillus pyocyaneus.

The pathological report on the section of sigmoid showed no evidence of new growth and the diagnosis was acute perforated diverticulitis. The patient was discharged February 2, 1929.

This patient, since his discharge from the hospital, has been in good health, has daily stools with the aid occasionally of mineral oil. There is a hernia at the site of the incision in the left lower abdomen.

The speaker remarked that since 1849 when diverticula of the colon were first described by Cruveillier many have written on the subject. Colonic diverticula are not uncommon. Inflammatory changes with subsequent complications occur in about 17 per cent. of the cases of diverticulosis observed clinically, and about 14 per cent. observed at necropsy. In a group of 227 cases malignancy was associated in only 1.8 per cent. However, it should be emphasized that the surgeon is frequently deceived at the time of operation as to the true nature of the lesion and that a certain diagnosis cannot be made until the specimen has been examined microscopically.

Doctor Weeder believes that there is a certain group of cases reported as five-year cures of carcinoma of the colon without microscopic verification that were actually diverticulitis.

DR. DAMON B. PFEIFFER recalled a patient in whom diverticulitis was discovered by X-ray, in which there were some pelvic symptoms, and the surgeon, in his exploration, finding nothing in the pelvic organs themselves to account for this, resected a large portion with a disastrous result. The sigmoid is not a very good place to resect on account of the blood supply. It is not necessary to operate always. Even when a mass presents itself if it can be controlled, it is part of wisdom in certain cases to let that mass subside. He has seen a very considerable mass, the size of a fist, practically disappear on treatment. Of course, in the case of perforation, there is no choice but to operate.

DR. GEORGE P. MULLER said that a sigmoid diverticulum may produce a rapidly acute peritonitis which may be mistaken easily for appendicitis. The speaker thought that most surgeons have the conception of diverticulitis as a condition producing a gradual obstruction of the sigmoid, thus resembling carcinoma or a perforating retroperitonitis and forming a suppurative mass

## CARBUNCLE OF THE KIDNEY

in the groin. He had had three or four of the acute variety, all of which were diagnosed as pelvic appendix and in all a normal appendix was found, a greatly thickened cæcum felt, and thus the true nature of the infection discovered. In two of these patients, transitory fistulæ occurred. It is difficult to know what to do in these cases but probably the best treatment is simply to place good drainage.

## TORSION OF THE GREAT OMENTUM

DR. JOHN JEFFRIES (by invitation) read a paper with the above title, for which see page 761.

DR. WILLIAM B. SWARTLEY recalled the case of a woman, over sixty years of age, who was received at the Chestnut Hill Hospital with the diagnosis of acute cholecystitis. At the operation the gall-bladder was not found to be the cause of the acute condition, although it did contain stones but a part of the omentum was found to be firmly adherent to the peritoneum covering the abdominal wall just below and lateral to the gall-bladder. This part of the omentum after it had been separated from the abdominal wall was found to be dark in color and to be the seat of three complete twists at the base of the darkened or gangrenous area. This piece of omentum was resected; the gall-stones were removed, the gall-bladder drained and the patient made an uneventful recovery.

## CARBUNCLE OF THE KIDNEY

DR. BENJAMIN LIPSHUTZ read a paper with the above title, for which see page 766.

DR. GEORGE M. LAWS remarked that his interest in the subject of cortical infections of the kidney began with the publication of Dr. George E. Brewer, who presented the picture of fulminating infections that often demanded immediate life-saving operation. Later, as the condition became better known, it was learned that, in some cases, the infection is comparatively mild, and it was difficult to determine whether early operation was required. The speaker is sure he has seen mild cortical infections clear up entirely without operation and he is still sometimes in doubt as to the treatment to be applied. It is important to remember that there are two types of kidney infection: that the colon bacillus type is manifested by pyelitis or pyelonephritis, and that the coccal type causes cortical lesions, including carbuncle, and complications such as perinephric abscess.

Doctor Laws studied the available cases of perinephric abscess from the standpoint of urinary findings, but as the essayist has said, the findings were often meagre and the study was not fruitful until he learned from various writers of the value of the stained smear in addition to the urine culture. The ordinary culture of the urine does not always give a true bacteriologic report because the cocci may not grow, or may be overgrown, by the colon bacilli.

DR. GEORGE P. MULLER remarked that Doctor Lipshutz had omitted to mention that condition occasionally called Brewer's Kidney or acute unilateral

hæmatogenous suppurative nephritis. Following Brewer's paper many years ago there were a great many reports of similar cases and as the speaker remembers the cases in his own experience, they were practically the same except for their acuteness as those described by the essayist. In view of the tendency to do conservative procedures upon the kidney, it should not be difficult to do a partial nephrectomy in the chronic type of case mentioned by Doctor Lipshutz instead of complete nephrectomy. That this can be done is shown by one of the case reports from the literature in which a bilateral condition was treated by nephrectomy on one side and nephrotomy on the other. In such cases Doctor Muller would suggest that the wound be unsutured entirely and the cavity filled with gauze in close contact with the infected kidney and perirenal valve.

DR. BENJAMIN LIPSHUTZ, in closing, said that he had attempted to present only the chronic group of cases. Brewer directed attention to the acute cases in which there is a violent clinical picture with evidence of septicæmia and urged immediate surgery. The infections known as chronic carbuncular type persist over a long period of time, lasting not infrequently for months. One of the cases presented symptoms for three months. In the acute type of case the infection is overwhelming. Multiple small abscesses may be associated with the carbuncular type. Some of the cases show multiple carbuncles. In the early stage the carbuncular type is localized and appears from the mildness of symptoms, as a different type of infection, from that observed in acute diffuse hæmatogenous group. He agreed with Doctor Muller that if the case is subjected to operation at an early stage, conservative surgery consisting of resection of the abscess and packing of the resultant cavity is the desirable procedure. The wound cavity should be left open and free drainage established, otherwise a septic wound may be the result.

#### CÆCAL DRAINAGE IN ACUTE SUPPURATIVE APPENDICITIS

DR. GEORGE M. DORRANCE remarked that every surgeon can recall numerous instances where a patient after an appendicectomy with drainage was practically moribund but upon developing a fæcal fistula promptly began to improve. Abdominal distention with its accompanying discomfort is a frequent and disagreeable complication of suppurative appendiceal cases. These facts led him to believe that in selected cases cæcal drainage should be established after the removal of the appendix.

Regarding indications and contra-indications the essayist said that there is a tendency to drain fewer cases of appendicitis and he is in accord with this view. The cases, however, in which all surgeons agree on drainage are where there is free pus in the abdominal cavity. In his opinion, these should have, in addition to the usual drainage of the peritoneal cavity, cæcal drainage. In cases of localized appendiceal abscess there is a question as to whether or not, in addition to the usual drainage, cæcal drainage is advisable. In these cases, if the appendix has been removed, when the abdomen is opened he employs this procedure. Doctor Dorrance's technic is as follows:

After removing the appendix a rubber catheter (Number 20 French) is inserted through the appendiceal stump well into the cæcum and held with a purse-string suture of Number 2 chromic catgut. The cæcum is then allowed to drop back in place and the usual drains are introduced. When the patient is returned to his bed, he is placed in the Fowler position. A small amount of fluid may be immediately introduced by the drip method or any way one wishes. Every three hours the catheter is sucked out with a syringe to remove the fluid intestinal contents, or they are allowed to flow out. The catheter is removed, or comes out of its own accord, in from four to eight days, depending upon the progress of the case.

The advantages are that one secures drainage of the cæcum which prevents post-operative distention. It permits removal of a large amount of liquid fæcal material and permits fluid, salt solution, glucose, etc., to be introduced into the colon at a place where absorption can readily occur—an improved Murphy method of getting fluid into these patients. In cases where nature would cause a fæcal fistula to develop, the surgeon by establishing cæcal drainage offers a much smaller opening and a stormy convalescence is prevented. It is seldom necessary to do a secondary operation to close the fistula. Secondary hernia do not seem to be more frequent than in drainage cases he has had in the past.

DR. I. S. RAVDIN said that in 1927 Clyde Wilson reported a large number of cases treated by this method with a remarkably low mortality. Since then he has used it a number of times and it seems to have a very definite field of usefulness. He puts the small catheter through the appendiceal stump and uses a long linen suture from the base of the appendix and threads a tube over that so that when the catheter is removed, if any further drainage does occur, there is a ready passage for it. There is no doubt the patient will receive and take much larger quantities of fluid by this method than any other. The speaker does not recall any complications in the cases in which he has used this method.

DR. DAMON B. PFEIFFER said that certainly cæcostomy is unnecessary in the average condition of acute appendicitis. The vast majority of these cases get well without any sort of drainage. The fact that it permits the administration of large amounts of fluid, in itself, would be no indication in most instances. The speaker could think of only one condition in which cæcostomy would be of any value, and that is in a pelvic collection with partial obstruction of the pelvic colon. In that condition it might be very valuable.

DOCTOR DORRANCE, in closing, said that he had observed no disadvantages from the use of this procedure, but has seen many advantages. Fluid can be administered directly into that portion of the bowel from which the maximum absorption takes place. He is sure that distention is less; it decompresses the colon. He uses salt solution and not glucose. He does not advocate the routine employment of cæcostomy, but in bad cases with pus in the peritoneal cavity he does advocate its use. He has had no complications and can see no objections to the method.

# BRIEF COMMUNICATIONS

## EXTENSIVE RESECTION OF SMALL INTESTINE

FROM a study of the reported cases in which extreme resections of intestine have been performed, it is noted that 220 centimetres (six feet, seven inches) is the limit which can be removed without serious danger of post-operative metabolic disturbances, as indicated by hunger, thirst and diarrhoea.

According to Treves', experience from 100 autopsies the average length of small intestine in the male is 680 centimetres (twenty-two feet, six inches) and in the female nearly fifteen centimetres (six inches) more. This excess, however, might not be confirmed in a larger series. In the male the extremes were 970 centimetres (thirty-one feet, ten inches) and 470 centimetres (fifteen feet, six inches) while in the female they were 890 centimetres (twenty-nine feet, four inches) and 570 centimetres (eighteen feet, ten inches). If these figures be accepted, the removal of 200 centimetres will average about one-third of the total length and may reach near one-half.

The report of results appears to justify resection up to and beyond the usually accepted safety point when necessary as an emergency to save life, but probably does not justify it to remove massive malignancy when the prognosis is essentially poor. According to Brenizer (May, 1929), there have been eighty-three cases of extensive resection of small intestine reported with 85.7 per cent. operative recoveries and 65.5 per cent. showed good functional results.

Metabolic studies show the first effects of the operation is an increase in excretion of the nitrogenous, fatty and carbohydrate elements of the food. However, compensation is usually established. In experimental studies on dogs, Flint reports a compensatory hypertrophy of the remaining portion involving mainly the mucosa and consisting of an increase both in the number and size of the villi, although this has not been found in human cases as yet.

Cathcart suggests that these recoveries may be accounted for by the fact that the small intestine rarely functions to the limit of its capacity but possesses a great reserve power, which will, under favorable dietary conditions, be equal to the larger amount of added work. It is true that there is present in every organ of the body reserve tissue which may be called upon for functional purposes in an exigency. On the other hand, compensation will break down under adverse conditions, such as faulty diet, which could be well borne by normal individuals.

In view of the small number of cases reported and the opportunity of observing the following cases over a considerable period of time they are considered of sufficient importance to report.

## DIFFERENTIATION OF BRANCHIAL CYSTS

CASE I.—E. B., white, male, aged twenty-one years, yeoman in Coast Guard, uses alcohol in moderation and smokes pipe occasionally; does not use drugs.

*Family history.*—Father and mother living and well. Two brothers living and well, none dead. Three sisters living and well, none dead. No history of tuberculosis, cancer, insanity, heart or kidney trouble in family.

*Previous personal history.*—Has not had any tropical service. Believes he has had all the ordinary childhood diseases and malaria. His right arm was broken when a child. Had gonorrhœa one year ago. No operations. *Chief complaint.*—Pain in right side.

*Present history.*—States pain came on very suddenly about 9 p. m. May 10, 1929, across lower abdomen and gradually localized in right side. Describes pain as sharp, and cramp-like in character. Nauseated and vomited several times without relief. Bowels not constipated. No increase in urinary frequency or blood in urine. Has never had a similar attack.

Physical examination reveals a fairly well nourished and slightly developed white male lying in bed quietly. Weight, 145 pounds; height, five feet, eleven inches; blood-pressure, 110/70. Examination negative except for marked tenderness and rigidity in right lower quadrant. Rebound tenderness present. Rectum examination negative.

*Laboratory findings.*—Urine, trace of albumin, granular casts, numerous pus and few blood-cells. Blood count, 30,000 white blood cells with 86 per cent. neutrophiles, 12 per cent. small mononuclear, and 2 per cent. large mononuclears. Wassermann: negative. Coagulation time, five and one-half minutes.

Patient was operated on under ethylene anæsthesia and an acute gangrenous appendix removed. The following day the abdomen was slightly distended but otherwise convalescence was uneventful. On the twentieth day he began to have pain in the abdomen with nausea and vomiting. Blood chemistry, non-protein nitrogen 42.6 milligrams per 100 cubic centimetres and chlorides 445. Diagnosis of intestinal obstruction was made and patient operated under ethylene anæsthesia relieving numerous adhesions and kinking of small bowel, which obliterated the lumen. The patient was in very poor condition and the wound had to be closed as quickly as possible. Convalescence from this operation was also uneventful and the man rapidly regained strength. On the fortieth day following this, however, he had a recurrence of the same symptoms and was again operated upon under spinal anæsthesia with removal of twelve feet of gangrenous small bowel leaving approximately four inches of ileum and eight feet of jejunum. At this time urine was negative, blood showed 4,700,000 red cells, 26,400 white cells with 83 per cent. neutrophiles and 17 per cent. small mononuclears. Hæmoglobin 70 per cent. non-protein nitrogen was twenty-four milligrams per 100 cubic centimetres blood and chlorides 445. Transfusion of 500 cubic centimetres of whole blood was given by direct method.

During convalescence the man complained of occasional attack of diarrhœa which was easily controlled. For two months following operation indican was present in urine and undigested fat and starch in fæces.

After convalescence thirty days' sick leave was granted and on return from this patient was discharged ready for duty. He complained of no digestive disturbance and weighed 140 pounds, undigested fat was still present in fæces.

Six months following operation patient was again seen. He had no complaint and was doing his regular duty. He weighed 145 pounds. Examination was negative except for potential weakness of abdominal wall in operative scar. Urine was negative for indican. Fæces were still positive for undigested fat. This apparently was not affecting his nutrition or general health in any way. At this time X-ray showed barium having reached splenic flexure of the colon in six hours. The small intestine is massed together in the pelvis and freely movable. The colon is practically empty after twenty-four hours. He was again seen eleven months after operation and appeared in good health. At that time he was doing his duty in the Coast Guard and offered no complaint.



## BRIEF COMMUNICATIONS

CASE II.—E. W., colored, male, aged forty-one. Occupation, merchant seaman. Occasional use of alcohol and tobacco.

*Family history.*—Negative. *Previous personal history.*—Has not had any tropical service. Had measles and mumps when a child, no injuries. Had gonorrhœa a few years ago.

*Present history.*—States that one week ago he was constipated and took several cathartic pills following which he developed pain in lower abdomen, more marked on right side. Was not nauseated and did not vomit. When pain persisted he took several doses of salts without relief. Does not have increased frequency nor blood in urine. Never had similar attack before but has had attacks of indigestion.

*Physical examination.*—Well-nourished and developed colored male. Weight, 150 pounds; height, five feet, seven inches; blood-pressure, 128/74. Examination negative except for slight rigidity of right lower quadrant and tenderness on deep palpation.

*Laboratory findings.*—Urine, negative; white blood count, 9,500; Wassermann reaction, 4 plus.

Under ethylene anæsthesia a gangrenous appendix was removed. The appendix was retrocecal and the cæcum was so inflamed and brittle that a portion was removed to make closure. The patient was having an uneventful convalescence when on the tenth day he began to have pain and distension of abdomen with nausea and vomiting. At this time blood showed 8,150 white cells with 77 per cent. neutrophils, 20 per cent. small mononuclears, 1 per cent. large mononuclears and 2 per cent. transitionals. Non-protein nitrogen was thirty-nine milligrams per 100 cubic centimetres of blood and chloride content 463. There was a palpable mass in the right side of the abdomen. He was again operated upon under ethylene anæsthesia for intestinal obstruction with removal of eight feet of small intestine, cæcum, and four inches of ascending colon. After a hard convalescence he gradually gained weight and had none of the complaints of hunger, thirst and diarrhœa usually associated with large intestine resection. At no time was indican found in the urine. Undigested fat was present in the feces up to the time of discharge.

When discharged barium enema showed the colon filled without difficulty. The rectum and sigmoid were slightly dilated and the haustra of the sigmoid were not as well defined as they should be. Three months after operation non-protein nitrogen was 31.8 per cent., blood sugar 86.2 per cent. and chloride content 495.

It is interesting to note that extensive resection apparently was not having any effect on blood chemistry in this case.

Ten months after operation he was seen. He offered no complaint, except occasional attack of diarrhœa. He was working as a waiter. He weighed 148 pounds, being well-nourished for his height.

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## DIFFERENTIATION OF BRANCHIAL FROM OTHER CERVICAL CYSTS BY X-RAY EXAMINATION

Cysts in the neck can usually be recognized as such by the ordinary criteria of physical examination. Occasionally, however, they may be confused with inflammatory conditions, especially tuberculous adenitis, and elude identification. Branchial cysts not uncommonly are subject to periodic attacks of inflammation which accounts in large measure for the frequency

with which they escape detection. With the almost universally practised procedure of treating tuberculous adenitis with conservative measures, it is important that patients with cysts in the neck be spared the loss of time and disappointment afforded by the treatment accorded patients with tuberculous adenitis.

Two patients have come under my observation in which cervical cysts passed under the guise of other pathologic lesions over a long period of time. One patient was temporized with over a two-year interval under the impression that he had tuberculous adenitis or a "cold abscess" from a tuberculous spondylitis which gave few physical signs. The other patient had been given a diagnosis of tuberculous adenitis and repeated aspirations had been practised when the "abscess threatened to break down."

When the patients were first seen at the University Hospital, the diagnosis of branchial cyst was entertained because of the location of the swelling in each instance. A definite diagnosis, however, could not be made by the usual criteria of physical examination. Following aspiration through a hypodermic needle and the injection of a medium opaque to the X-rays, the diagnosis of cyst was easily made in both instances on X-ray examination. The needle was left *in situ* following the injection and the injected medium was re-aspirated after the inspection of the film.

A much neglected but valuable piece of evidence in the recognition of branchial cysts that has been significantly emphasized by Hamilton Bailey<sup>1</sup> is the presence of cholesterol crystals on microscopic examination of the aspirated content. The high lipoid content frequently imparts a shimmer or yellowish sheen to the fluid when it is placed in an open basin. Though not invariably present, these findings are practically conclusive for the existence of a branchial cyst.

X-ray examination with employment of the method suggested here should be of great practical help in all cases of cervical swellings of obscure or indeterminate origin. The finding of a sharply circumscribed limitation of the opaque injection medium on the X-ray film is pathognomonic of a cyst. In the presence of a tuberculous lymph node that had given rise to suppuration or "cold abscess" from a tuberculous spondylitis, the opaque medium would be seen to dissect along the natural tissue planes in an irregular fashion.

Even at operation there may be considerable doubt as to the identity of a branchial cyst. Before employing the procedure described here I have been misled at operation by the presence of considerable lymphoid tissue surrounding the cyst and its universal adhesion to surrounding structures, into believing that I was dealing with a tuberculous lymph node; and in cysts that have been the seat of repeated active inflammation, the information obtained by inspection and microscopic examination of the aspirated content is frequently without special value. A röntgenogram after the injection of an opaque medium, however, gives indubitable evidence as to whether or not a cyst is present.

## REFERENCE

<sup>1</sup> Bailey, Hamilton: Physical Signs in Clinical Surgery, p. 34, Wm. Woods and Co., 2d ed. 1930.

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## A GUARD FOR THE GIGLI SAW

A SIMPLE DEVICE TO PREVENT THE GIGLI SAW FROM COMING IN CONTACT WITH ANY OF THE TISSUES EXCEPT THE BONE TO BE CUT

DURING the amputation of a limb, a great deal of time and effort is consumed and unnecessary trauma produced in an attempt to retract the skin, muscle and fascia as high as possible in order to saw off the bone at the desired level. Very often the adjoining tissues are shredded, the retracting towels and drapes are torn, and even the hands of the willing assistant are caught during the to-and-fro motion of the saw. Particularly is this true when dealing with more than one bone such as in an amputation of a leg, in sawing off the metacarpal or tarsal bones or in rib resection. The cramped condition of the parts hinders retraction and free motion of the saw. It was the attempt to deal with such a case that prompted the writer to improvise a simple device to obviate these difficulties.

Recently the writer did a high amputation of the thigh in a very obese woman. This was necessitated because of gangrene extending up to the thigh as the result of an embolus complicating cardiac disease. Following the amputation, a good deal of sloughing of the soft parts ensued because of the poor circulation. The patient, however, survived the operation and six weeks later the wound appeared clean and granulating. As a result of the sloughing, there developed a big cone-shaped cavity about three inches deep with the bone projecting in its depth for about one inch. (Fig. 1-C.) It was deemed advisable to remove the projecting portion of the bone to expedite healing and avoid a painful stump.

The writer was in a quandary as to the method of removing the bone without causing unnecessary trauma to the soft parts, the projecting bone being quite deep in the cavity. Bone cutting forceps would leave ragged edges. It was inaccessible to the ordinary saw because of its depth and it would necessitate undue trauma, additional incisions and forcible retraction of the soft parts in order to gain access to the bone. The Gigli saw was deemed most practical. Even this, however, was not feasible for in order to be able to work the saw at such a depth, one would have to cut down and separate the soft parts to allow for its to-and-fro motion. Whereupon an idea occurred to the writer to use a guard for the saw as presented in the illustration.

The idea was to pass the Gigli saw through a hollow metal tube, the loop of the saw to pass over the stump of the bone to be removed, in a manner similar to the application of the ordinary tonsil snare. The hollow

tube would act as a guard, retractor and guide and thus prevent injury to the soft parts and enable the saw to be held at any desired level of the bone. A search for a hollow tube however, at this time proved unsuccessful. The writer then spied a Bell stethoscope which was being used for blood-pressure in spinal anæsthesia. This appeared to be most ideal for the purpose as it fulfilled all the requirements. It has a wide bell-like opening at one end and

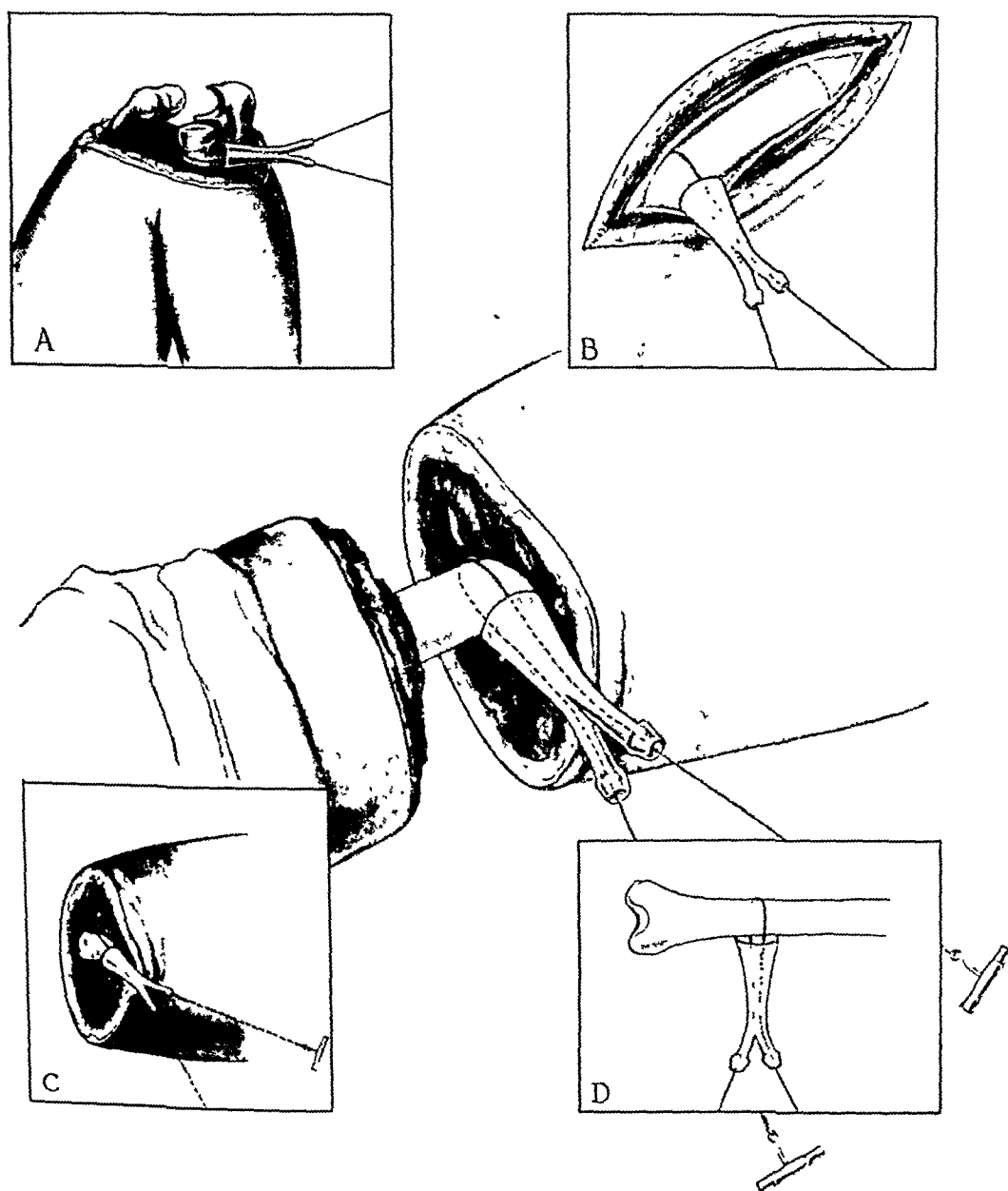


FIG. 1.—Guard for the Gigli saw. Amputation at middle of thigh. Bone to be sawed off with Gigli saw, using bell of stethoscope as a guard. Note the ease with which loop of saw can be placed at any level of the bone with the aid of this guard. A—Excision of head of radius. B.—Resection of rib. C—Secondary removal of stump of femur. All with aid of guard which makes retraction of soft parts unnecessary. D—Note close contact of guard held against bone which serves to steady bone during the sawing motion.

two Y branches at the other end through which the Gigli saw could readily be threaded and serve the purpose above described.

The projecting bone was thus removed in less than a minute with no more than twenty motions of the saw. The writer was greatly surprised at

the rapidity, ease and exactness with which the bone was sawed off with the aid of this improvised guard for the Gigli saw. By holding the guard firmly against the bone it was steadied and the disconcerting to-and-fro motion of the stump ordinarily produced by the pulling of the saw was avoided. By referring to the illustration, one can readily see the practicability and usefulness of a hollow metal tube for this purpose. A modification of this guard as to shape and size may prove of value, depending upon the location, size and thickness of the bone to be dealt with. Naturally in sawing off a very thick bone, a wider and more flattened tube may be advantageous, while working in a narrow space such as resection of rib or mandible, a smaller tube of a somewhat different shape may be useful. The principle however, is the same in all cases, namely, to utilize a hollow tube for the purpose.

The tube helps to steady the bone, guide the saw, retract the soft parts and guard them from being injured. It thus greatly enhances the usefulness of the saw, enables one to sever almost any bone without fear of direct injury to surrounding parts, eliminates unnecessary and forcible retraction of the adjoining structures with its incident devitalization, and it makes the work of the surgeon and his assistants less arduous and more effective. A single attempt will readily convince the surgeon of the usefulness and practicability of the writer's guard for the Gigli saw.

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#### A METHOD FOR MAKING A SATISFACTORY FISTULA AT ANY LEVEL OF THE GASTRO-INTESTINAL TRACT\*

It is well known that it is difficult to maintain in a normal physiologic condition animals in which a fistula has been established in any portion of the gastro-intestinal tract. The difficulties are mainly those associated with loss of the contents of the part of the tract in which the fistula was produced, with the resulting decrease in nutrition and possible excoriation around the stoma. The seriousness of these complicating factors depends on the portion of the digestive tract from which the contents are lost. Contents lost from the lower portion of the digestive tract, as from the lower portion of the ileum and colon, is usually not serious, although decrease in weight associated with some injury to the surface of the skin around the fistulous opening does occur. However, loss of secretion from the upper part of the digestive tract, as the stomach, jejunum, or upper portion of the ileum, usually proves rapidly fatal.<sup>1, 2, 3</sup> or productive of marked and rapid decrease in the nutrition of the animal associated with considerable injury to the surface of the skin by the discharged digestive juices. In any event, animals from which any considerable amount of gastro-intestinal contents are being lost are not altogether suitable subjects for physiologic study.

In some of our investigations it was necessary to obtain specimens of the contents of the gastro-intestinal tract at various levels repeatedly over

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## GASTRO-INTESTINAL TRACT FISTULA

long periods of time. After various methods had been tried, the following procedure was devised and has proved satisfactory to us. Essentially the method consists in isolating a short loop of the terminal portion of the ileum and employing it to make the fistulous tract to the portion of the gastro-intestinal tract in which it is desired to tap.

All operative procedures are performed under ether anaesthesia with the employment of surgical technic. The abdominal cavity is entered through a low median-line incision, and the terminal portion of the ileum is exposed. This portion of the intestine is easily recognized by the longitudinal artery

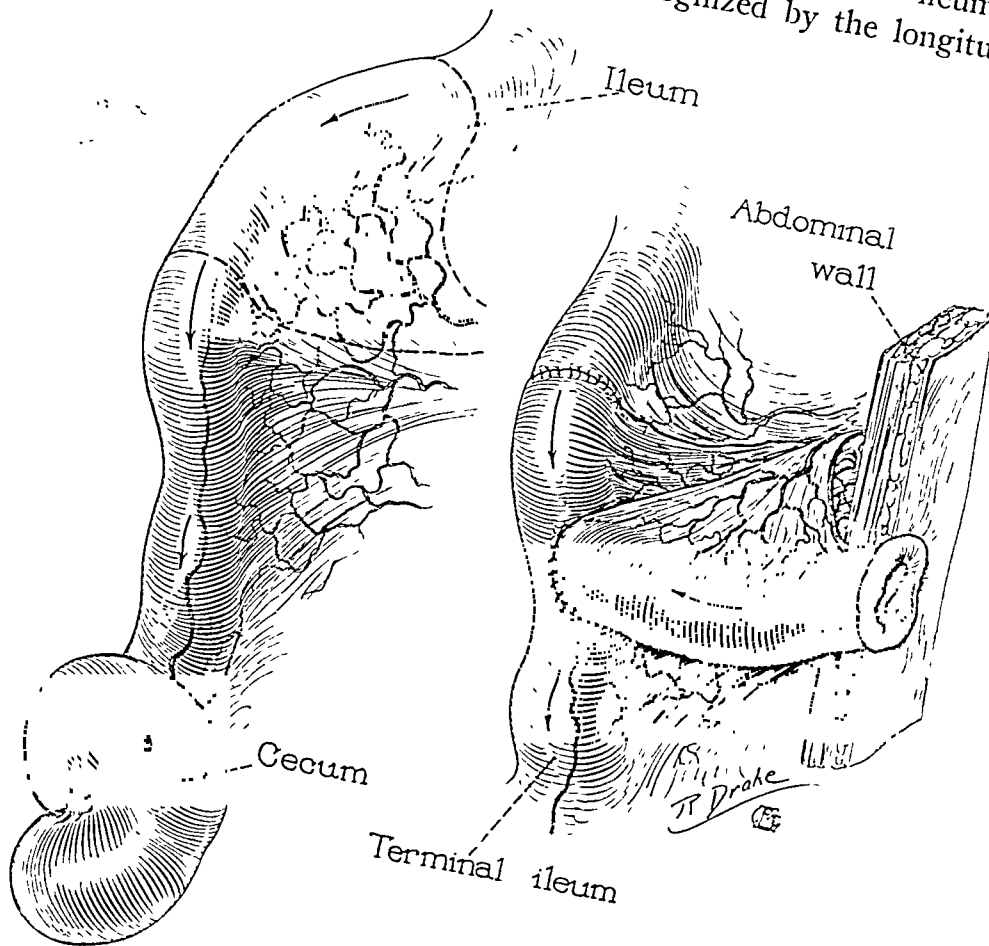


FIG. 1.—The essential steps in the procedure. The fistula was in the terminal portion of the ileum. It is readily seen that the same procedure can be used for any other portion of the gastro-intestinal tract.

coursing on its wall so prominently in the dog. The first loop of ileum cephalic to the termination of the longitudinal artery is carefully isolated. This loop should be from 15 to 20 centimetres in length and should have a long mesentery. Before the lumen of the intestine is opened the portion of the digestive tract in which the fistula is desired should also be exposed. Both sites of operation should be carefully packed off. The isolated loop is clamped at each end, and the intestine is severed so that the clamps are left on the ends of the isolated loop. The continuity of the intestine is reëstab-

lished with either end-to-end or side-to-side anastomosis. The isolated loop is then gently transferred, without stretching its mesentery, to the other exposed section of the digestive tract. End-to-side anastomosis is done between the distal end of the transposed loop of ileum and the other exposed area of the digestive tract at the exact site at which the fistula is desired. The free end of the transposed loop is then drawn through a stab wound, and sutured to the skin (Fig. 1).

This procedure makes it possible to have a fistulous tract lined with mucosa from the surface of the body to any portion of the gastro-intestinal



FIG. 2.—Double fistula. The lower opening leads into the pyloric region of the stomach and the upper opening leads into the duodenum. Each loop was anastomosed about 2 centimetres from the pyloric sphincter on its respective sides. Hundreds of samples of gastric and duodenal contents were secured from these fistulas. The perfect condition of the mucosa and adjacent skin surface may be noted. These fistulas have been under observation for more than twenty months.

gastro-intestinal tract, in excellent condition for several years. It is also possible to tap the gastro-intestinal tract at two or more points, that is, to make a fistula of the stomach and of the duodenum, or any portion of the lower part of the intestine (Fig. 2).

There are a few points in technic that we have found worthy of consideration. It is essential, as in most gastro-intestinal operations on the dog, to be careful to pack off all the sites of operation on the tract before the lumen of the intestine is opened and soiling from gastro-intestinal contents is per-

Since the waves of peristalsis in the transposed loop pass from the surface of the skin to the lumen of the tract, leakage does not often occur. The passage of a suitable catheter through the transposed loop into the lumen of the digestive tract permits both the withdrawal of specimens of the gastro-intestinal contents and the injection of food and other substances. It has been found possible to secure from sixty to one hundred samples of intestinal contents through such a fistula, or to maintain a continuous flow by allowing the catheter to remain in place during the course of ten hours without having any serious leakage occur. We have found it possible to maintain animals, with fistulas at various portions of the

mitted. Care should be taken in the end-to-side anastomosis to make a large opening, as the only difficulty so far encountered has been gradual stenosis at the site of this anastomosis. We have also found it advantageous to use fine catgut for this particular anastomosis. It is obvious that a loop of the jejunum or upper portion of the ileum could also be transposed. However, the loop from the terminal portion of the ileum suits the purpose better.

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## BOOK REVIEWS

OPERATIVE GYNECOLOGY. By HARRY S. CROSSEN, M.D., and ROBERT J. CROSSEN, M.D. Fourth edition, 8vo.; cloth; pp. 1054. C. V. Mosby Company, St. Louis, 1930.

This, the fourth edition of Doctors Crossen's "Operative Gynecology" shows the usual attention to detail characteristic of the authors—even the preface is valuable and instructive. By giving credit where credit is due they have really internationalized their book. This is well exemplified in the chapter which includes vesico-vaginal fistulæ. The work has been amplified to twenty-four chapters. The teaching value of the work is greatly enhanced by the profusion of the excellently executed illustrations. It is evidently the production of men who have thought as they have worked. Their consideration of the development of the proper procedure gives an authoritative atmosphere to that which they recommend and practise. Their finality and deductions are convincing and their attitude is wholesome.

The psychological effect upon the reader of their reporting their fatal cases is of great value to everyone. Their illustrative cases in the text are very instructive. Those of us who have been unfortunate enough to injure a ureter during the performance of a hysterectomy have all gone through the stage of identification of the ureter by the introduction of ureteral catheters pre-operative.

The authors' consideration of mooted points throughout the book relieves the reviewer of any criticisms against their regard for detail. The only real criticism is the use of proctoclysis, post-operatively, in cases of ectopic gestation.

In chapter XIV on the external genitals and vagina they have included the lymphatics of the vulva, the review of which, including those of the whole pelvis, from an anatomical standpoint is of great help not only in the consideration of malignancy but also for any infectious process. Regarding malignancy of the external genitals, the Doctors Crossen have produced a remarkably clear set of ideas, especially from the standpoint of classification. Chapter XV on disturbances of function necessitates being familiar with their book on "Diseases of Women."

The inclusion of chapters on appendectomy, the intestinal tract and hernia show the finished gynæco-abdominal surgeons. The attitude on femoral hernia is especially to be recommended.

ALBERT M. JUDD.

PIERSOL'S HUMAN ANATOMY. 9th Ed. Revised under supervision of G. Carl Huber, M.D., Sc.D. J. B. Lippincott Co. 1930.

During the last two decades there have appeared numerous articles extolling the new "physiological surgery" as opposed to the former "anatomical

surgery." This has led some, particularly those who have been medical students during this period, not only to emphasize physiology, which of course is highly commendable, but also to belittle the importance of anatomy. Medical schools have been forced to shorten the course in anatomy from two years to one, principally because of the vast amount of new knowledge to be imparted in all the other departments, rather than because of any lessened importance of anatomy itself. Although we feel that, in general, medical education has greatly progressed during this period and that students are better fitted to handle themselves, still it does seem that the anatomical foundation is not quite so strong among recent graduates as formerly. This situation is particularly evident in surgery; for although no one will deny the importance of physiology, still both physiology and surgery must be based on a fundamental knowledge of anatomy.

For this reason the appearance of the new ninth edition of Piersol's *Human Anatomy* is of significance, and it is to be hoped that it may stimulate added interest in this important subject. From the first edition in 1907 through the eighth edition in 1923, Doctor Piersol carried the tremendous load of editorship of this huge volume, aided, in the writing of the text, by Drs. Thomas Dwight, Carl A. Hamann, J. Playfair McMunich, and J. William White. The editorial work of this monumental text-book has now been entrusted to Dr. G. Carl Huber, under whose efforts the ninth revision now appears. Doctor Huber has been assisted by members of the staff of the Department of Anatomy of the University of Michigan, and, particularly in the revision of the "Practical Considerations," by Dr. Eldridge L. Eliason, Professor of Clinical Surgery of the School of Medicine of the University of Pennsylvania.

Descriptive gross anatomy shows but little change between editions, so that revision of subject-matter has been confined largely to the sections dealing with histogenesis of the lymphatics and primary veins, the peripheral nervous system, and the fibre-paths of the central nervous system. The main editorial revision has been the more complete introduction into the text of the Basle anatomical nomenclature. Fortunately for those who were brought up on the less-consistent English terminology both appear throughout. This more complete use of the Basle system in one of America's outstanding anatomical text-books is evidence of the progress the Basle Congress has made since 1907. In the original preface Doctor Piersol said:

The constant aim of the editor has been to use the simplest anatomical terminology, and preference has always been given to Anglicized names, rather than to the more formal designations. Although in many cases the modifications suggested by the new terminology have been followed with advantage, consistent use of the Basle nomenclature seems less in accord with the conceded directness of English scientific literature than the enthusiastic advocates of such have demonstrated.

This acceptance today of the international anatomical terminology seems but another indication that the world, with communication improving in

every way, is becoming more closely knit. The pagination of the eighth edition has also been maintained, so that guides and outlines based on the last edition may still be used without change.

The general appearance of the new edition is entirely unchanged. There are 2,104 pages, with 1,734 illustrations, 1,522 of which have been selected from more than 2,000 original drawings made largely from the dissections of Dr. John C. Heisler. Those who are familiar with these fine illustrations know that it has been the editor's aim to present the actual appearance of parts rather than to schematize them.

In this edition most of the line-drawing diagrams of the central and sympathetic nervous system tracts have been redrawn, corrected, and extended to comply with the textual revision. A new colored plate showing the development of the reticulo-endothelial cell or histocyte, in bone marrow, has been inserted to illustrate the new description of "The Development of the Corpuscular Elements of the Blood." The monophyletic theory, that all the blood cells, both red and white, are derived from a common mother cell, is very briefly outlined, Marimow's work being particularly alluded to.

Unlike descriptive gross anatomy, which is now fairly standardized, "Practical Suggestions" require constant revision, because of the continuous rapid advances in surgery. Doctor Eliason has been responsible for this part of the work and has revised, and in places added to the "Suggestions." It is readily understandable that with pagination fixed and sections of space limited to former allotments, extensive changes are almost impossible. These "Suggestions," however, are very important, probably most so because of the interest they add to the pabulum which most medical students consider only too dry.

In closing it is entirely unnecessary to add any recommendation of this pre-eminent volume to the reader, who already undoubtedly knows it as an old friend. Doctor Huber and his staff, however, certainly deserve the thanks of the entire profession for the tremendous amount of time and energy required in editing this new edition.

WILLIAM H. FIELD

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## TUMORS OF THE CAROTID BODY

REPORT OF TWELVE CASES INCLUDING ONE OF BILATERAL TUMOR\*

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THE MAYO CLINIC

TUMORS of the carotid body, which are exceedingly rare, may give rise to few symptoms and yet demand formidable surgical procedures for their eradication. Two admirable reviews of the literature recently have appeared: one by Bevan and McCarthy, in 1929, reporting a case of their own and noting from the literature 133 other cases, and one by Talman, in 1928, noting 177 cases reported in the literature and adding a case of his own. Adding ours to this number, and six other cases, <sup>3, 4, 7, 12, 13, 15.</sup> which we have found in the literature, not reported by the authors named, brings the total to 196 cases.

Our interest was stimulated to review the cases at the Mayo Clinic by the occurrence of a case in which tumor of the carotid body was bilateral and in which operation was successfully performed. So far as we have been able to ascertain, this is the only case of bilateral tumor of the carotid body reported in the literature, in which the tumors appeared simultaneously, although Lund<sup>10</sup> mentioned a case in which a second tumor appeared in the opposite side of the neck twenty-nine years after removal of the first one.

The first anatomic description of this body was made by Von Haller<sup>1</sup> in 1743, under the name "ganglion minutum," and in 1797, Andersch described it as occurring at the bifurcation of the common carotid artery, terming it "ganglion intercaroticum." Luschka<sup>1</sup> added a description of the microscopic structure in 1862. The first description of a tumor of the carotid body in the American literature was that of Scudder,<sup>9</sup> in 1903. In 1906, Keen and Funke contributed a complete survey of the literature. Among the earlier cases reported were those of Da Costa<sup>6</sup> and Cathcart.<sup>5</sup> In 1881, Stieda<sup>9</sup> described the carotid body as a triangular collection of cells, connected by means of fine, fibrous strands with the oral epithelium on one end and with the thymus on the other. Embryologically, it is supposed to be derived from the epithelium of the pharynx, from the walls of the blood-vessels, from nerve tissue, or from the sympathetic ganglion cells of the carotid plexus. Physiologically, little is known of it. Indeed, it is not known whether it should be classified as fulfilling the function of an endocrine body or just

\* Read before the Southern Surgical Association, December 9, 1930.

what function it exerts. In 36-millimetre embryos, this collection of cells is round and is no longer connected with the aforementioned structures; nevertheless Stieda maintained that the carotid body arises from them. In the sheep embryos, 10 to 11 millimetres in length, the body first appears as a thickening from the posterior portion of the horizontal branch of the branchial cleft, which is opposite the portion of the cleft from which the thymus develops.

The view that this body is of epithelial origin was supported by Rabl,<sup>8</sup> whereas Bonn<sup>8</sup> was inclined to believe that the structure develops in the accessory thyroid gland. Fischels<sup>8</sup> maintained that the embryologic origin of the carotid body is from the tissues lying between the approximately ectodermal and entodermal layers, denying, thus, its development from epithelial tissue. Katschenko<sup>8</sup> was the initial advocate of the view that the adventitia of the internal carotid artery near the bifurcation of the common carotid is the origin of the gland. This thesis is somewhat supported by the views of Arnold<sup>8</sup> and Waldeyer, and others. The first appearance of the structure in embryos 14 millimetres or more in length is of an ellipsoidal body composed of loosely woven, richly cellular connective tissue, and Paltauf<sup>8</sup> agreed with Katschenko that the anlage is connective tissue rather than epithelial tissue. Kohn<sup>1</sup> maintained that the body is distinctly neurogenic and that it develops from the embryologic ganglion cells of the intercarotid plexus, a view in which he supported the hypothesis of Luschka.<sup>1</sup> Marchand<sup>8</sup> also observed that in embryos of four months the body was surrounded by loosely woven connective tissue in which were many blood-vessels and nerves.

Anatomically, the glomus caroticum, or the ganglion intercaroticum, is an ovoid body, approximately 5 millimetres long, 3 millimetres wide, and 1.5 millimetres thick. Its customary situation is the median and deep aspects of the upper end of the common carotid artery at its bifurcation into the internal and external trunks. Occasionally, it is found distinctly on the posterior side of the bifurcation. It is a firm body, of grayish or brownish color, with a distinctly fibrous capsule, and contains a hilum at which its arterial blood supply enters. Capsular prolongations into the body itself divide it somewhat indistinctly into lobules, which, in turn, are further subdivided by delicate strands and capillaries, forming alveolar spaces which contain the cellular elements. The capillaries have been described by some as almost sinusoidal; they are of large diameter, but thin-walled. There is, with increasing age, a piling-up of connective tissue and an increase in the number of blood-vessels, at the expense of the epithelial elements. Finally, as the person grows into adult life, the carotid body undergoes changes which eventually make it recognizable as a distinct anatomic structure. The characteristic cellular elements which distinguish it are the polygonal cells. Their protoplasm is finely granular, and the nucleus, which is ovoidal and comparatively large, contains a small amount of chromatin. Some cells which are found in the stroma and the lobules stain brown when treated with chromic acid. To these chromaffin cells Mulor<sup>8</sup> attributed an important functional

significance, calling attention to the fact that similar cellular elements are observed in the suprarenal glands, coccygeal body, the hypophysis cerebri and the abdominal sympathetic ganglia.<sup>2, 11</sup> Marchand<sup>8</sup> postulated that although the structure of the gland is difficult to determine, it is composed of two essential elements: Blood-vessels and cells. In the lobules the branches form capillaries, producing a pattern which conforms to the structure of the gland, as described by Arnold,<sup>8</sup> who mentioned that the essential part of the carotid body consists of the glomeruli which are formed by the capillary network. The polyhedral or ovoidal cells are intimately related to the blood-vessels, so much so, in fact, that Marchand was strongly inclined to regard them as derivatives of the capillaries.

When tumors affect this body, they become lobulated or globular and sometimes take on the appearance of a small kidney when they grow to sizable proportions. If they remain globular, they may push up into the notch of the carotid vessels, increasing the angle, and finally may advance forward to lie on the vessel. The consistence is increased and the mass is firm, usually, although occasionally it may be brain-like to the touch. The tumors are always encapsulated and resemble somewhat, when removed, foetal adenomas or tumors of the parathyroid gland, although blood-vessels are a conspicuous element in their make-up and are observed in all parts of the capsule abundantly.

*Pathology.*—Pathologically, these tumors are often designated by such names as "adenoma," "endothelioma," "perithelioma," "paraganglioma," "neuroblastoma," "sarcoma," and simply "carotid body tumors." The last term seems a sensible one until pathologists are able to agree on a better term. Paltauf<sup>8</sup> suggested "perithelioma" as the most common pathologic type among these tumors on account of their origin. The tumor cells contained in the alveoli are without definite arrangement and sometimes are positively malignant, infiltrating the walls of the vessels and the surrounding tissues, and yet slow-growing and almost invariably without a tendency to metastasize. However, in Gilford and Davis' case, metastasis was into the liver, but these authors questioned the validity of the diagnosis and noted another patient of Moenchenberg, who died of papillary adenocarcinoma of the ovary after removal of the carotid body. Two of the patients in the group reported from The Mayo Clinic returned with possible metastasis to the brain; one patient had symptoms of a brain tumor and the other of epilepsy, but these conditions were not verified by necropsy. Lund mentioned one case in which metastasis to the liver was found at necropsy. With the exception of these cases, distant metastasis has not been noted, although occasional observers have reported cases which involved the regional lymphatic structures. Bevan and McCarthy noted that in 17 per cent. of the whole group, definite malignancy had occurred in the tumors of the carotid body, and that nearly 9 per cent. of the patients had definite recurrences. Malignancy, however, is uncommon. The recent articles in the literature, which have been reviewed thoroughly, agree that about 80 per cent. of tumors of these bodies

are benign and that about 20 per cent. are malignant. Careful analysis of all reported cases, as our experience in the clinic has verified, will indicate that many tumors, called tumors of the carotid body, are, in reality, not carotid tumors at all, but belong to some other group of malignant growths of the neck.

The general structure of the tumors of the carotid body described is nearly always the same. The epithelial cells are packed in an endothelial-lined alveolus, the size of which varies in different tumors. In our case of bilateral tumor, one growth was composed very strikingly of this alveolar arrangement, whereas, on the opposite side, it was almost absent. The first tumor looked like an adenoma or like hyperplasia of the body, whereas the other tumor had somewhat the character of a neurofibroma.

The characteristic structure of a tumor of the carotid body is that of an alveolar perithelioma, with its whorls or *zell-ballen*. The cells are polyhedral and granular, and are arranged in compact groups, with or without lumens surrounded by endothelium. Some tumors are vascular, due to the numerous large vessels and blood spaces, lined by prominent endothelial cells, which sometimes protrude into the lumens in masses. The amount of stroma varies; in some it is scant and in others it is dense.

Because of lack of definite knowledge as to the character of these tumors, we have classified our cases as examples of benign and malignant tumors of the carotid body. We have considered as malignant those in which there was much variation in size of the cells: Large, single, or multiple hyperchromatic nucleoli; the presence of mitosis, and invasion of the tumor itself into its capsule.<sup>14</sup>

*Symptoms.*—The paucity of symptoms in the early stages of tumor of the carotid body is characteristic. Usually the patient notes a lump in the neck which is symptomless and scant attention is paid to it. The mass is movable, frequently, and varies in size from a small tumor which is freely palpable, to one like that which appeared in our case in which the mass was bilateral and about 7 centimetres in diameter. As the mass enlarges, usually pulsation is observed through it because of its attachment to the blood-vessels, and this false symptom makes its distinction from an aneurism of the carotid artery, or of one of its branches, essential. The type of pulsation noted, because of the close association of the tumor with the free carotid vessels, is an interesting phenomenon. Almost always this pulsation is present but it lacks the expansile quality of an aneurism, and although there is no pathognomonic symptom, this pulsation is typical. Rarely are there associated symptoms, such as the thrill and bruit which are produced by aneurismal masses. The mass may be grasped and moved from side to side, and the skin is not attached over it. Differential diagnosis usually is difficult and frequently is not made correctly. Aneurism of the carotid vessels probably is the first thought presenting itself, but some type of lymphoma, lymphosarcoma or tuberculous invasion of the lymph nodes of the neck must be eliminated. Lesions of the thyroid gland, and branchial cleft cysts likewise have to be

considered, but most often the tumor can be distinguished from these. In the early stages the tumor is mobile and remains so until it becomes attached to the surrounding tissues, when symptoms of pressure occur. Pain is conspicuous by its absence, and is rarely noted, and tenderness to palpation is not observed. Vagal pressure, causing fainting spells, is not uncommon and in three cases which were reported the Stokes-Adams' syndrome was present. Interference with the recurrent laryngeal nerve causes, in a great many instances, hoarseness and other changes in the voice, dysphasia, dyspnoea, and so forth. The astonishing length of time over which some of the tumors persisted, which were found later to be tumors of the carotid body, indicates the proneness of these tumors to be benign rather than malignant. In some of the cases, the condition had persisted for as long as thirty-five years or more.

Among our twelve patients there were seven women (58.3 per cent.), and five men (41.6 per cent.). The ages ranged from twenty-three to sixty-eight years. Usually the tumors occur in middle life, in the third or fourth decade, although this is by no means uniform and many patients are younger. The youngest patient, according to Bevan and McCarthy, was aged seven years. We have not been able to obtain the report of this particular case but Sinyshin reported the age of one patient as nine years.

The diagnosis is rarely made pre-operatively. Only when the tumor is uncovered and microscopic examination confirms the suspicion that there is a tumor at the bifurcation of the carotid artery is this rare entity identified.

The magnitude of the surgical procedure for removal of tumors of the carotid body is influenced, in the main, by the necessity of ligation of one, two or three carotid vessels. The densely adherent tumor, which affixes itself in the carotid notch in such a manner as to make its dissection impossible without removal of some of the carotid vessels, is removed with difficulty and danger in proportion to the patient's age and the necessity of sacrificing not only the carotid vessels but adjacent structures, such as the cervical lymphatic apparatus, or the vagus nerve. The latter may be resected without much additional risk, but increase in the difficulty may be sufficient to increase the mortality. Ligation of the common carotid artery in adults, particularly those who are in the latter half of middle age and beyond, is an extremely serious procedure, which carries with it a high rate of mortality, well recognized by all surgeons, ranging from 30 to 65 per cent. In our series of cases it was necessary to ligate the common carotid artery in three, and all of these patients succumbed in the first forty-eight hours. The external carotid artery of other persons was ligated twice but without undesirable sequelæ or fatality. The tumor was excised in all of the cases. Of the nine patients who survived the operation, seven are living and well. In eleven of our cases, five tumors were found to be malignant and six benign at the time of operation. In the case in which the tumors were bilateral that of the left side was found to be malignant and that of the right, benign, making a total of six malignant and seven benign tumors of the carotid body.



## ABSTRACTS OF THE TWELVE CASES OBSERVED AT THE MAYO CLINIC

CASE I.—A woman, aged thirty-four years, had noted enlargement of the thyroid gland for fifteen years. There had been no noticeable increase in size in the six years previous to her admission. Operation was performed April 5, 1913, and revealed multiple thyroid adenomas and also a mass, which was adherent to surrounding structures, lying high in the neck, toward the angle of the jaw. The pathologic diagnosis was malignant tumor of the right carotid body, measuring 7 centimetres, 5 centimetres, and 4 centimetres in various diameters, associated with multiple adenomas of the thyroid gland. The patient died in August, 1913, in a condition of paralysis. In this tumor there were masses of epithelioid cells lying in an endothelial stroma. Many mitotic figures were present.

CASE II.—A woman, aged fifty-three years, had had a lump in her neck for six years. It had increased slowly in size and had produced local symptoms of pressure. The clinical diagnosis was probable cyst. Operation was performed January 19, 1915. The pathologic diagnosis was benign tumor of the right carotid body, measuring 6 centimetres, 2 centimetres, and 2 centimetres in various diameters. The patient died January 23, 1915, of thrombosis of the middle cerebral artery. The tumor consisted of numerous, small, whorl-like masses of epithelioid cells lying in endothelial-lined spaces. The stroma was rather heavy, consisting of fibrous hyaline tissue.

CASE III.—A man, aged twenty-six years, first noticed a lump seven years previous to his admission; it grew slowly and then decreased in size three years later with massage. The clinical diagnosis was lymphocele (70 per cent.) and carotid body tumor (30 per cent.). Operation was performed March 17, 1915. The pathologic diagnosis was malignant tumor of the left carotid body. The patient returned in 1925 with epilepsy, which had been present for the previous four months. A gangrenous appendix and the tonsils were removed in 1925. The tumor was composed of groups of epithelioid cells lying in endothelial-lined spaces, and also large, whorl-like bodies. In certain regions there was a papillary appearance, with larger, deeply-staining cells in dense, fibrous connective tissue, and with some invasion of the capsule of the tumor.

CASE IV.—A woman, aged forty-five years, first noticed an enlarged gland in the right side of the neck in 1913. At that time she had earache and pain through the face. She had had influenza in 1918, with pain in the cheek bones, over the eyes, and in front of the ears. Following this, jaundice, with pain over the liver, appeared. A painless lump appeared under the right jaw and gradually enlarged. In the six months previous to her admission at the clinic she had lost fifteen pounds in weight. The clinical diagnosis was post-influenzal tuberculosis. Operation was performed February 12, 1919. The pathologic diagnosis was as follows: Tumor from bifurcation of carotid artery, malignant tumor of the carotid body; cellular tumor with tendency to form *zell-ballen* but little true formation of them; cells varying in size, with many containing prominent, deeply-staining nuclei, and some cells with multiple nuclei. By September, 1919, recurrence had not taken place.

CASE V.—A woman, aged fifty-two years, had a lump on the left side of the neck, about 2.5 centimetres in diameter and of unknown duration. She also had a branched renal stone. Operation was performed August 20, 1919. The pathologic diagnosis was benign tumor of the carotid body, 3 centimetres, 2.5 centimetres, and 5 centimetres in various diameters. The patient died on the day following operation from hæmorrhage. The tumor was composed of many small, whorl-like masses of epithelioid cells. Scattered in the stroma were a few of these cells.

CASE VI.—A man, aged sixty-eight years, had had a tumor of the right side of the neck for eight years previous to his registration at the clinic. He remembered having a small kernel at the angle of the jaw thirty-two years previously. It had not enlarged until he had the "grippe." The clinical diagnosis was tumor of the carotid body or mixed tumor of the salivary gland. Operation was performed September 20, 1920. The pathologic diagnosis was benign tumor of the carotid body, 7 centimetres, 6 centi-

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metres, and 4 centimetres in various diameters. The patient died five days following operation, of bilateral bronchial pneumonia and softening of the brain. The tumor consisted of epithelioid masses arranged in radial fashion and also in the characteristic whorls. There were many cells of variable size and deeply-staining nucleoli.

CASE VII.—A woman, aged thirty-five years, had had a growth, about 2.5 centimetres in diameter, at the right angle of the jaw for one year. It did not increase in size and there were no symptoms. Operation was performed August 15, 1921. The pathologic diagnosis was malignant tumor of the carotid body, composed of a large number of masses and whorls of epithelioid cells, with a tendency to invade the capsule. The patient returned in August, 1930, complaining of dizziness, headache, black spots before the eyes, and stiffness of the muscles of the neck. She had had a lump in the right thigh for one month which proved to be a fibrosarcoma.



FIG. 1.—Bilateral tumors of the carotid body.

CASE VIII.—A man, aged thirty-eight years, first noticed a small lump on the right side of the neck two and a half years previous to his registration at the clinic. It increased in size. Tonsillectomy was performed. Some aching and soreness occurred. The clinical diagnosis was branchial cyst or tuberculous glands. Operation was performed March 21, 1923. The pathologic diagnosis was benign tumor of the carotid body 6 centimetres, 4 centimetres, and 3 centimetres in various diameters. The tumor consisted of rather heavy fibrous, hyaline tissue, containing a few collections of epithelioid cells lying in endothelial-lined spaces, and it contained many of the characteristic, whorl-like masses.

CASE IX.—A woman, aged thirty-six years, first noticed an "enlarged gland" on the right side of the neck in 1922. Following tonsillectomy it disappeared for six months. Three months later the lump again appeared. The clinical diagnosis was branchial cyst or tuberculous glands. Operation was performed July 29, 1924. The pathologic diagnosis was benign tumor of the carotid body 4.5 centimetres, 3 centimetres, and 2.5 centimetres in various diameters. The tumor consisted of large masses of

epithelioid cells arranged in radial fashion, without any definite whorls, producing the appearance in cross section of a papillary tumor of the urinary bladder.

CASE X.—A man, aged thirty-seven years, had a tumor of the left side of the neck of four years' duration. Just previous to his registration at the clinic, it had increased in size more rapidly than formerly. He refused treatment, but returned five years later, at which time the tumor had increased considerably in size, and had encroached on the pharynx and hypopharynx. Operation was performed March 27, 1925. The pathologic diagnosis was malignant tumor of the carotid body, 6 centimetres, 5 centimetres, and 3 centimetres in various diameters. By 1927 there was no recurrence. The tumor was composed of groups and of many whorl-like masses of epithelioid cells lying in endothelial-lined spaces. Scattered in the stroma were epithelioid cells of various sizes. An occasional mitotic figure was present and there was a tendency of the tumor to invade the capsule.

CASE XI.—A woman, aged forty-nine years, had a mass in the left side of the neck, attached to underlying structures and not producing symptoms. She had a stone in the ureter. The clinical diagnosis was branchial cyst. Operation was performed December 3, 1926. The pathologic diagnosis was benign tumor of the carotid body, 4.5 centimetres, 6 centimetres, and 6 centimetres, in various diameters. The weight was 85 grams. The tumor was encapsulated, grayish-brown, spongy, and edematous, with cystic, hemorrhagic portions. The centre was firmer, and yellowish-brown.



FIG. 2.—Tumor of carotid body, right side, 5 centimetres, 4.5 centimetres, and 3 centimetres in various diameters. The weight was 35 grams. The tumor was oval, encapsulated, semisolid, and reddish-gray.



FIG. 3.—Tumor of the carotid body, left side, 7 centimetres, 6 centimetres, and 6 centimetres, in various diameters. The weight was 85 grams. The tumor was encapsulated, grayish-brown, spongy, and edematous, with cystic, hemorrhagic portions. The centre was firmer, and yellowish-brown.

metres long and 2 centimetres wide. The tumor was composed of solid masses of epithelioid cells and whorl-like structures of similar cells lying in endothelial-lined spaces, clothed in a fibrous capsule.

CASE XII.—A man, aged forty-nine years, registered at the Mayo Clinic in June, 1929. He came because of swelling on both sides of the neck (Fig. 1) which he first had noticed as nodules about 1 centimetre in diameter, ten years previously. He had had an attack of parotitis seven years previously which had lasted three days. Both nodules increased in size slowly until, at the time of removal, they appeared as rather soft tumors, about 4 to 7 centimetres in diameter, the larger of which was on the left side. The tumor removed from the right side (Fig. 2) measured 5 centimetres, 4.5 centimetres, and 3 centimetres in various diameters, and weighed 35 grams. It was oval, encapsulated, semisolid, and of a reddish-gray color. On section it was semisolid, homogeneous, dark reddish-brown, and had the appearance of an undifferentiated foetal adenoma of the thyroid gland. The tumor removed from the left side (Fig. 3) measured 7 centimetres, 6 centimetres, and 6 centimetres in various diameters and

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weighed 85 grams. It was oval, encapsulated, and on section it was grayish-brown, spongy, and œdematous, with cystic hæmorrhagic portions, varying in size. In the centre, it was firmer, and the color was yellowish-brown.

Microscopically, the tumors were composed of blood spaces, varying in size, and

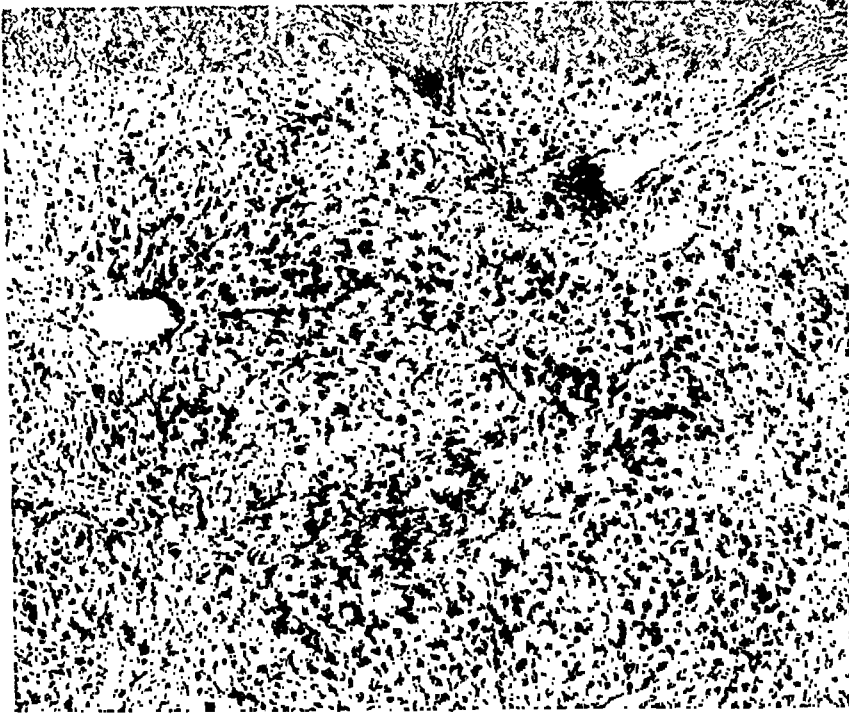


FIG. 4.—Microscopic picture of tumor from the right side. Diffuse epithelioid cells lay intermingled in the endothelial connective tissue; also, there were many larger, irregular spaces.

alveoli lined by endothelium containing large, polyhedral cells with large, oval nuclei, with deeply staining, coarse and fine granular protoplasm. In the unfixed tissue, stained by polychrome methylene blue, these cells closely resembled those present in adenomas

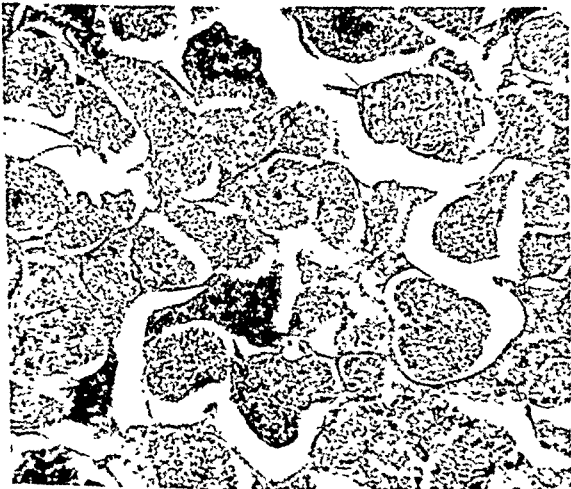


FIG. 5.—Microscopic structure of most tumors of carotid body. The characteristic perithelial or whorl formations in the tumor of the left side.

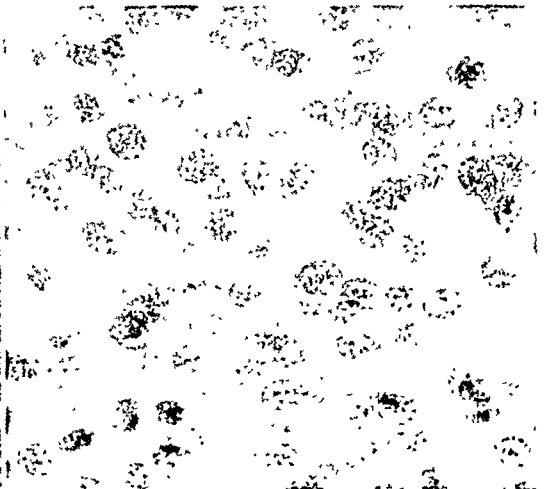


FIG. 6.—High-power magnification of cells composing epithelial element or tumors of the carotid body. Rather dark, granular protoplasm is present (x900).

of the parathyroid gland. However, the histologic design distinguished this tumor from other similar tumors. Many of the alveoli were reinforced by connective fibrous tissue.

The cells which composed the tumor on the right side (Fig. 4) lay in a rather diffuse, fibrous, endothelial stroma and also in whorl formation. In this tumor there

was very little of the alveolar structure so characteristic of tumors of the carotid body, whereas, on the left side (Fig. 5), the predominant feature was the alveolar arrangement. The cells varied in size and had poorly defined outlines. In some there was a suggestion of a spinous process, giving the appearance of a nerve cell. The nuclei were oval or round, varying in size; some were very large. The nucleoplasm was finely and coarsely granular, and stained from a pale pink to a deep purple. Occasionally there was seen a deeply-staining, prominent nucleolus and a mitotic figure (Fig. 6). Fresh sections, stained with polychrome methylene blue, and fixed sections stained with hæmatoxylin and eosin were studied. Special staining was not done; therefore, the presence or absence of chromaffin cells was not determined.

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# SURGERY OF THE PHRENIC NERVE IN TREATMENT OF INTRACTABLE HICCUP

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ONE of the most distressing post-operative complications in abdominal surgery is intractable hiccup. It may be mild, yielding to the simpler forms of treatment, or it may be extremely severe with interference of respiration and deglutition. There is no doubt that in the severe form the patient can and will gradually go down hill and die from exhaustion.

It is the purpose of this paper to describe the course of a case of intractable hiccup appearing in a patient who had been operated on for a perforated duodenal ulcer. The usual medical treatment for hiccup having failed over a period of eleven days, the phrenic nerve was crushed with permanent relief of the condition. Only temporary relief was previously obtained with novocaine block and traction.

CASE I.—The patient, forty-one years of age, a male telephone operator, was admitted to Bellevue Hospital with a diagnosis of perforated duodenal ulcer. He was operated on within a few hours and the perforation closed. He ran a post-operative temperature of 102° to 103° F. for five weeks. The origin of this fever could not be determined. Thirty-nine days post-operative he developed signs of a right lower lobe pneumonia which were confirmed by X-ray.

At this time the patient complained of severe hiccup. This complication continued without intermission both day and night for eleven days. All the usual remedies were tried without the slightest success; ether injections, inhalation of carbon dioxide, tracheal compression, digital compression of the phrenics, and injections of large doses of morphine and hyoscine.

The patient was gradually going down hill from exhaustion. He was cyanotic, his pulse was weak and rapid. There was considerable difficulty in swallowing and moderate dyspnoea. The cause of the hiccup was thought to be a diaphragmatic pleurisy of the right side, causing reflex stimulation of the right phrenic nerve. Therefore, under a local anæsthetic, the right phrenic nerve was exposed and isolated in its course on the scalenus anterior. The rate of hiccup at the beginning of the operation was twenty-two times per minute. Two cubic centimetres of 1 per cent. novocaine were injected into the nerve. The hiccup stopped immediately for the first time in eleven days with great relief to the patient.

As it was thought that the novocaine block would merely afford temporary relief, a stout silk ligature was passed about the nerve, the ends brought out of the wound and attached with adhesive tape to the skin. The wound was then closed. Eight hours later the hiccup recommenced, the effect of the novocaine having apparently worn off. The rate of hiccup now was sixteen times per minute.

Traction was then exerted on the nerve by means of the silk ligature and immediately the hiccup stopped. During the night, for a period of eight hours, traction was used three times due to return of the hiccup. Relief from this method lasted about two hours.

As neither anæsthetization nor traction gave permanent relief, the nerve was pulled into the reopened wound and crushed with a stout clamp. Following this procedure there was complete and permanent relief of the hiccup. Fluoroscopy at this time showed an immobile right diaphragm.

The further course of the patient displayed a continued temperature. X-ray examinations made during the next few weeks showed a spread of his pulmonary lesion characteristic of tuberculosis. His sputum became positive for tubercle bacilli. He ran a downward course and died three months post-operative, of his tuberculosis.

The experimental evidence obtained in this case as to the blocking of nerve impulses through the phrenic nerve is worthy of emphasis. Two cubic centimetres of 1 per cent. novocaine controlled spasm of the right side of the diaphragm for about eight hours. The same result for two hours was obtained by moderate traction of the nerve.

Hiccup is an extremely complicated mechanism that is far from being fully understood. The characteristic sound of hiccup is produced by a spasm of the diaphragm causing a sudden inspiratory movement with closure of the glottis. Apparently in the milder forms of hiccup the diaphragm is the chief respiratory muscle involved. However, in the more severe forms some or all of the accessory muscles of respiration may be involved.

These groups of muscles apparently have a common centre of control: the respiratory centre in the medulla. This centre is subject to numerous reflex stimuli. It may respond to stimuli from the mouth, pharynx, larynx, lung, skin, gastro-intestinal tract and diaphragm. It is undoubtedly acted upon by certain toxic products in the blood as in the hiccup of uræmia from chronic nephritis.

It seems probable in the case just reported that the diaphragmatic pleurisy caused a reflex stimulus of the phrenic nerve on that side. That the phrenic nerves contain sensory fibres we know because of the pain experienced by the patient during phrenic resection.

In every case of hiccup in which there is spasm of the diaphragm, it seems logical to believe that this spasm can be relieved by interrupting the course of nerve impulses through the phrenic nerves. However, when the hiccup includes the other muscles of respiration, which are numerous, then crushing or avulsion of one or both phrenics may not give complete relief.

*CASE II.—Bilateral Phrenic Avulsion.* Woman aged thirty-five, a singer by profession. Admitted to the French Hospital January 16, 1931, service of Dr. H. C. Falk. Complaining of persistent hiccup of five years' duration. The only occasions during this period when there was cessation of the hiccup were during sleep.

The patient gave a history of an attack of grippe five and one half years before, which lasted some few months and was followed by typhoid fever. Soon after this the patient underwent a severe mental shock. The hiccup apparently started in the train of these events.

The woman is in apparently excellent health, but extremely neurotic. The hiccup occurs about 5 to 10 times per minute with severe attacks in which the rate rises to 140 times per minute. On fluoroscopy both sides of the diaphragm appear to be involved.

The etiology is extremely difficult to determine. Whether we are dealing with a post-encephalitic hiccup or one of an hysterical nature, it is impossible to say. This

patient had undergone for five years all the usual procedures for the relief of hiccup, with no results. On this admission avertin anæsthesia had to be given on nine different occasions to allow the patient some rest. As a last resort bilateral phrenic avulsion was done February 11, 1931, under local anæsthesia.

The patient hiccupped for about one hour the evening of the operation day; twelve times the second post-operative day, and since then has been entirely free from this complaint.

Phrenicotomy is an operative procedure attended with but little risk and certainly seems justifiable in those cases of severe hiccup in which the patient's life is endangered. This operation is today frequently performed in the treatment of chronic pulmonary tuberculosis. In the treatment of hiccup it becomes an emergency measure.

The relation of the phrenic nerve to hiccup was recognized at least as early as 1833 by Doctor Shortt<sup>1</sup> of Edinburgh who recommended blistering the surface of the neck over the origin and course of the phrenic nerves for intractable hiccup. He reported several successful cases treated in this manner.

Digital compression of the cervical portion of the phrenic is a common method of controlling hiccup and its successful use reported by Grognot,<sup>2</sup> 1885, and Leloir,<sup>3</sup> 1892.

Galvanic and faradic currents applied to the region of the phrenic nerves have been used and reported successful in the treatment of hiccup by Capriati,<sup>4</sup> 1898, and Regis and Debedat,<sup>5</sup> 1897.

It was not, however, until after Stuertz<sup>6</sup> and Sauerbruch<sup>7</sup> in 1911 demonstrated the possibility of an artificial paralysis of the diaphragm by section of the phrenic nerve that actual surgery was used to prevent hiccup.

In 1917 Kroh,<sup>8</sup> at a meeting of military surgeons, reported the successful novocaine treatment of ten cases of severe hiccup resulting from dysentery. He injected 10-20 cubic centimetres of a 1 per cent. novocaine solution into the scalenus anterior muscle three fingers above the clavicle at the outer border of the sternomastoid.

Goetze,<sup>9</sup> 1920, performed a temporary phrenic block in a young patient attacked by hiccup after appendectomy. He used the same technic as Kroh although independently. He was of the opinion that the anæsthetization lasts two to three hours. In the author's case anæsthetization lasted eight hours, but here 2 cubic centimetres of 1 per cent. novocaine were injected directly into the nerve.

Erkes,<sup>10</sup> 1921, reports bilateral injection in post-operative gastro-enterostomy hiccup of seven days' duration with relief.

Kummel<sup>11</sup> did novocaine injections in post-operative hiccup with success.

Payr<sup>12</sup> reported a left-sided injection with instant success.

Ghose,<sup>13</sup> 1926, reports a case of hiccup of four months' duration stopped with 1 per cent. novocaine injection, 2 cubic centimetres into both phrenics.

Jirasek,<sup>14</sup> 1925, reports a case of hiccup of ten days' duration cured by bilateral anæsthesia of the cervical sympathetics. He believes the sympathetic afferent portion of the phrenic nerve chiefly involved in hiccup. Because the sympathetic nerve conducts stimuli to the respiratory centre in reflex hiccup in cases involving all respiratory muscles or the diaphragm without them, he suggests severing the cervical sympathetic nerve at the cervical spot of phrenicotomy. He believes that bilateral phrenic avulsion is harmless in those not having exclusive abdominal respiration.



Actual section of the phrenic nerve was done in 1915 by Kroh, not for relief of hiccup, but for tetanic spasm of the diaphragm during tetanus, with complete success.

Kroh,<sup>16</sup> 1921, reported a case of a man forty-two years of age who had suffered for seven months from violent intermittent hiccup which persisted during sleep. Both phrenic nerves were injected with novocaine. The hiccup subsided and the patient went home, but returned in two weeks worse than ever and urging an operation. A right phrenicotomy was performed with temporary relief for three weeks; a left phrenicotomy was done without result; finally avulsion of the left phrenic was done with complete cure.

Kroh,<sup>16</sup> 1922, reported another successful case. He first tried bilateral novocaine injection for intractable hiccup with no success; he then did bilateral avulsion with a complete cure. The patient complained for several weeks of some dyspnoea on climbing upstairs or sleeping on his back. These symptoms, however, later cleared up.

It undoubtedly will not be successful in every case, as is evidenced by a few reports in the literature. Kappis,<sup>17</sup> 1924, reported bilateral phrenic avulsion in a woman who had previously had elsewhere bilateral phrenicotomy for hiccup of three years' duration. The hiccup, however, persisted. Physical examination showed no active participation by the diaphragm during hiccup, but a clonic contraction of the bilateral cervico-clavicular-thoracic muscles.

Lehmann<sup>18</sup> reports a case of post-encephalitic hiccup in a woman twenty-seven years old. This condition had persisted for two years in spite of morphine, scopolamine medication, hypnosis, novocaine injections into the phrenic nerve, faradization of the phrenics and finally bilateral phrenicotomy. Except when talking or sleeping the patient hiccupped forty times per minute. She requested a renewed operation. Bilateral phrenic avulsion was then done. X-ray showed complete bilateral paralysis of the diaphragm. Two days post-operative the hiccup returned accompanied by extreme dyspnoea that required laryngeal intubation. She gradually recovered but the hiccup returned.

From these failures we learn that the chance of cure with phrenic avulsion, in those cases in which the hiccup involves not merely the diaphragm but all muscles of respiration, is not very good. However, these people are willing to do almost anything, and if there is a slight chance of success, then phrenicotomy should be done.

Oehler,<sup>19</sup> 1922, reports a failure in a patient, a man, aged thirty-eight, recovering from a gastro-enterostomy, after resection of 1 centimetre of each phrenic nerve. The patient committed suicide. This was threatened by the author's patient unless relief was given.

We believe that failure should not be admitted following resection of a small piece of each nerve, but only after bilateral avulsion has been done. The reason for this is the frequent anastomosis of the phrenic with other nerve fibres below the point of resection, thus allowing nerve impulses a roundabout pathway to the diaphragm.

Dowman,<sup>20</sup> 1927, reports the relief of diaphragmatic tic following encephalitis by bilateral section of the phrenic nerves. The feature of this case was rapid breathing of a pure abdominal type, the rate being 130 a minute. On fluoroscopy there was a fluttering of the diaphragm, the contractions varying from 90 to 130 a minute. There was no evidence of thoracic movement. The right phrenic nerve was cut and the left frozen with ethyl chloride. Cutting the right phrenic had no influence on the rapid breathing, but as soon as the left phrenic was frozen the respiratory rate fell to twenty a minute, and the character of respiration changed from abdominal to thoracic type. The patient returned two months later with a respiratory rate of ninety. Fluoroscopy showed an

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immobile right diaphragm and fluttering of the left. The left phrenic was then divided with the respiratory rate dropping to twenty and complete cure.

Interest in this case centres on the apparent safety in cutting both nerves.

Freezing of the nerve with ethyl chloride has been done by Kroh,<sup>10</sup> Kuttner,<sup>21</sup> Goetze,<sup>9</sup> and others with some success. The effect apparently is of longer duration than that obtained in the novocaine block.

Steinke<sup>22</sup> in 1930 suggested traction on the phrenic nerve by means of a heavy silk ligature as a method of treatment for severe hiccup.

The plan carried out in the case just reported seems to be the most logical one. In intractable hiccup if all the usual methods of treatment fail, the patient should be fluoroscoped to determine which side of the diaphragm is involved. The phrenic nerve on the side involved should then be exposed under local anæsthetic and a stout silk ligature passed about it. The nerve can then be anæsthetized. This effect apparently lasts about eight hours. Following this, traction should be tried, and if it fails the nerve can easily be exposed and crushed. If at the time of operation, novocaine block and traction both fail, it should lead one to believe that there is nerve anastomosis below the site of section or blocking and the nerve should then be avulsed. If both sides of the diaphragm are involved, then both phrenics should be exposed and blocked either temporarily or permanently.

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# TRENDELENBURG'S OPERATION FOR PULMONARY EMBOLISM

REPORT OF A RECENT ADDITIONAL CASE

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IN THE ANNALS OF SURGERY, 1930, vol. xcii, No. 4, p. 498, Prof. Gunnar Nyström reported the cases of pulmonary embolism operated by him in the surgical department of the University Hospital in Uppsala. Since the publication of this paper, another case of the kind has been operated at the clinic. The embolus was successfully removed in this case also, and the circulation reëstablished, but the patient succumbed next day to a new embolus. Since it is important, as Nyström points out, to report all operated cases of pulmonary embolism in order to widen our knowledge and aid us in determining the indications, the technic of operation and the prognosis, I feel justified in relating this case, although its outcome was fatal, especially since so few cases have hitherto been reported. According to Nyström, only fifteen\* cases are reported in the literature, and of these, seven were definitely cured, while the remaining eight survived the operation only a short time. The case reported herein is thus the sixteenth published one to survive operation.

CASE.—Surgical Clinic Uppsala, 1930, No. 1634, married woman, aged fifty-eight. Patient rather corpulent. Had been in bed with fever up to  $39.5^{\circ}$  C. since June 2 with symptoms of cholecystitis. Good general condition. Cholecystectomy June 13. A stone the size of a thumb's end was found in the collum vesicæ fellææ. The first days after the operation the general condition of the patient was rather low, owing to a severe cough with much expectoration. June 18, five days after operation, her condition had improved, but the temperature still ran as high as  $38-38.4^{\circ}$  C., with a pulse rate of 80. As yet no clear symptoms of thrombosis. On this day, however, the patient had queer sensations in her left leg. She felt as if something were running in the leg. Some minutes later she fell back in her bed cyanotic, could give no answers to questions, and her pulse was no longer to be felt. The nurse at once made the diagnosis of embolism of the pulmonary artery. She therefore had the patient sent to the operating room at once, without awaiting the arrival of the surgeon on duty. When he arrived, the patient was unconscious; no pulse, respiration stertorous of pre-agonal type.

The operation was begun at once, at 3:40 P.M., without disinfection of the hands, the operator merely putting on sterile clothing and rubber gloves. The time between the onset of the alarming symptoms and the beginning of the operation cannot have exceeded four minutes.

*Operation* (Westerborn).—The incision was made without anæsthesia. No bleeding from the wound. Resection of the second and the third ribs. In the resection of the third rib, the parietal pleura was injured. The opening was occluded with a tampon. After the pericardium had been opened a rubber tube was placed around the aorta and the pulmonary artery. An incision of 10–12 millimetres was made in the wall of the

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\* By overlooking in reproducing the manuscripts, two cases in Nyström's list of surviving cases have fallen away. One case of Meyer's, dead of new pulmonary emboli twenty-five days after the operation, and one case of Crafoord's, discharged healed.

## OPERATION FOR PULMONARY EMBOLISM

latter after strangling the vessel by tightening the above-mentioned tube. The wound gaped without the use of retractors. With a forceps, a large embolus was extracted from each main branch of the artery. When the forceps was reintroduced into the lumen no further emboli were found, nor was there any thrombotic mass to be withdrawn by suction. The incision in the wall of the artery was closed with a clamp and the traction on the rubber tube was released. The vessel had probably been compressed 70-80 seconds at the most.

When the thoracic 'cavity' was opened, the heart beat quite feebly; only fibrillar twitchings could be observed. Immediately after the release of the mechanical hindrance the heart stood absolutely still, but on the injection of adrenalin into the aorta it began to move and very soon normal contractions appeared. The suture of the wound in the artery was rather difficult, the artery clamp having been placed very near the edge of the wound so that the sutures cut through. After readjustment of the clamp, the wound was perfectly closed and no blood escaped. Suture of the pericardium and the opening in the pleura. Skin suture. The internal mammary artery was covered.

The circulation had steadily improved after its reestablishment through the lungs, but not until the skin was sutured did the patient give any manifestations of pain. She did not answer questions, and did not regain consciousness until after she had been brought back to bed and the foot of the bed had been elevated. After an hour or so she was quite clear in her mind but for the next hour she was totally blind. At 7 o'clock in the evening her sight was normal and her pulse good. She recognized her surroundings and talked easily. Her breathing, however, was rather forced. Air was therefore aspirated from the left pleural cavity after which the respiration became quieter. During the night her condition was very good, she was 'mentally clear and her pulse calm. At 6 o'clock in the morning she became acutely worse; there was no palpable pulse, cyanosis and mental confusion. Exitus at 7:50 A.M.

The autopsy showed a large embolus obstructing the right branch of the pulmonary artery. Its size and position in the ramification of the vessels exclude the possibility of its having been overlooked at the operation. The embolus was somewhat adherent to the arterial wall. The place at which the artery had been sutured showed no thrombi. Both femoral veins were filled with thrombotic masses. Chronic myocarditis and incipient pneumonia of the left lung.

*Critique.*—In this case, the embolus obstructed the artery practically completely. That the operation could be made before it was too late was due solely to the fact that the nurse judged the situation correctly, and without waiting for the surgeon's arrival, notified the operating-room attendants and had the patient transported there at once. This prompt action and the circumstance that the necessary instruments are always sterilized and ready for use made it possible to start the operation three or four minutes after the onset of the embolus. When the heart was laid bare after about three more minutes, it had practically ceased to beat, and only fibrillar contractions of the heart muscle could be seen. In my opinion, the patient would have been dead inside of eight minutes after the onset if the operation had not intervened. This case is thus an example of the occasional possibility of making the operation and saving the patient even in these sudden cases, if the hospital staff is sufficiently watchful and the surgeon immediately at hand.

As for the technic of operation, the greatest difficulty in my opinion is connected with the preservation of the pleura, at least in cases like the one under discussion, in which the operation had to be performed very quickly.

The pleura is exceedingly thin and easily injured. If it is to be kept intact, the ribs to be resected must first be carefully detached. This may take a good deal of time, and I consider that when the patient is already almost in agony, it is more important to carry out the operation rapidly, even at the risk of injuring the pleura, than to lose time in carefully freeing it. In all other cases it is necessary to avoid injuring the pleura.

In most cases of pulmonary embolism, only part of the thrombus has loosened and entered the heart. There is consequently a great risk of new thrombi detaching and forming new emboli to the lungs. This risk is increased when the patient, on regaining consciousness, is restless, breathes stertorously and moves about more than is permissible in a case of thrombosis. The patient's transportation from the operating room to his bed naturally also augments the risk. In the case described here, the patient undoubtedly died of a new embolus to the lung, which was found at the post-mortem to obstruct the entire right pulmonary artery and extended all the way to its ramification. As a very large embolus was removed at the operation from each branch, and since no other thrombotic masses could be found either with the forceps or by suction, I believe it is out of the question that the embolus found at autopsy could have been overlooked at the operation. The probe was introduced far into both the branches of the pulmonary artery without meeting any obstruction. It is hard to decide when this new embolus developed. It is possible that it had already detached at seven in the evening, three hours after operation, as the patient's breathing became more forced at that time and she complained of greater pain in the chest. However, these symptoms were relieved by the aspiration of air from the left pleura. The embolus may also have developed the following morning, at the time the patient suddenly became worse, but the fact that the embolus was found at the autopsy to be partially attached to the wall argues more or less against this assumption.

At the autopsy, both femoral veins were filled with thrombotic masses, proving that the danger of new emboli had not been removed. The chances of a final cure are naturally greater in cases in which the entire thrombus has detached at one time than in those in which there has been only partial detachment.

Of the eight cases published that survived the operation but died sooner or later after it, there were one or two in which large emboli were found in the pulmonary artery at the post-mortem examination. Thus, Meyer's second case died of a new embolus to the lung twenty-five days after removal of the first one, and in Nyström's third case, in which the patient died thirty hours after operation, the cause of death was probably also a new embolus. The risk of new emboli is obviously very great, and should be kept constantly in mind in the post-operative treatment of the patient and the estimation of the prognosis after the successful performance of Trendelenburg's operation.

# LIGATION OF THE ABDOMINAL AORTA FOR ANEURISM OF THE COMMON ILIAC ARTERY\*

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THE purpose of this report, in addition to putting on record a case of relief of symptoms of aneurism following ligation of the aorta, is to make inquiry concerning the cure of aneurisms in general, and especially those involving the iliacs, aorta, and subclavian arteries.

There are up to now on record eleven cases of complete and partial occlusion of the abdominal aorta which survived the operation long enough to note the effect upon the disease. The cases herein reported make a total of thirteen. Of these there were seven cases of complete occlusion by ligatures of silk or cotton, and six of incomplete occlusion, five by aluminum bands, one by cotton tape. Eleven cases have had necropsies within from thirty-nine days to twenty-five months following operation.

All thirteen cases are reported since 1900 by ten American surgeons, eight of whom are living. Their painstaking studies have contributed greatly to the knowledge of the subject.

CASE No. 30-8024.—R. W., colored woman, age thirty years, admitted to St. Philip Hospital October 21, 1929, complaining of a "lump" in the lower abdomen, aching pain in the abdomen and right hip, radiating down the thigh. She had noticed these symptoms for only three weeks, but the pain was increasing, and the lump getting larger.

She was a healthy, well-nourished young woman, in whom there was a slightly tender tumor in the lower abdomen. The tumor was irregular in outline, immovably fixed, and palpable from the crest of the right ilium as far upward as within two fingerbreadths of the umbilicus and 2 or 3 inches to the left of the mid-line. There was a strong systolic expansile pulsation; no thrill could be felt, but a bruit could be heard.

Pulsation and blood-pressure in the right femoral and popliteal vessels was slightly weaker than in the left. The heart was not enlarged.

There were no signs of disease of the uterus, tubes or ovaries. The pulsating tumor was plainly felt by the finger in the vagina. X-ray of the pelvis and upper thighs showed no abnormal shadow, nor bone disease. Measurements at the groins showed the right thigh to be 24 inches, the left 22 inches in circumference. The blood Wassermann was strongly positive, the urine examination negative. *Diagnosis.*—Aneurism of the right common iliac artery.

After ten days in bed, operation was performed as follows:

Under spinal anæsthesia a long incision was made at the outer edge of the right rectus muscle, making special effort to preserve the integrity of the deep epigastric artery. With the peritoneal cavity open there was found a tumor the size of a partially flattened coconut, irregular in outline, located behind the peritonæum, densely adherent, fixed, extending from the right side of the bony pelvis nearly over to the sigmoid and exhibiting forcible and expansile pulsation. Coursing over the tumor could be seen the right ureter and many dilated veins. Neither of the iliac arteries could be identified.

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\* Read before the Southern Surgical Association, December, 1930.

Much effort was made, after incising the overlying peritoneum, to locate these vessels and after a time we found an artery the size of an adult finger located just to the left of the mid-line 2 inches or more above the promontory of the sacrum. Slightly above this point there was seen a small branch of the large artery (inferior mesenteric), going into the meso-sigmoid. When at this time, while an assistant had his fingers under the



FIG. 1.—Ligation of the abdominal aorta for large aneurism of the common iliac artery.

sterile sheets one on each common femoral artery, we made pressure on the large artery (aorta), there occurred immediate cessation of pulsation of both femoral arteries and of the tumor, and the tumor diminished in size

Another effort was made to identify the common iliac arteries, but these were so extensively covered by the tumor, which was densely adherent, that we were unable to

do so without unjustifiable risk of hæmorrhage. Upon making pressure sufficient for partial occlusion of the artery, there was noticed an intense thrill in the tumor, and when the artery was completely occluded the thrill and pulsation disappeared. The large vessel (aorta) was then gently separated from surrounding structures sufficiently to allow the passage of a large-size, curved hæmostat under the artery, for the purpose of drawing the ligature through. The artery was ligated with a coarse silk ligature, sufficiently tightly to obliterate completely the lumen of the artery, but not, we hoped, to crush its wall. After waiting about five minutes it looked as though the ligature might promptly cut through the vessel wall. We then placed over the first ligature in exactly the same position, a large ligature of twisted umbilical cord rope. This is about the size of a match stick and made of cotton. It was placed just tightly enough to obliterate the lumen of the vessel but not to crush the vessel wall. It was tied in a double straight knot, the ends cut close, the peritoneum lightly sutured over the ligature and vessels and the abdominal wound closed. In closing the abdominal wall we noted some venous bleeding and tied the deep epigastric vein. The artery was not injured nor ligated. The operation had consumed over two hours, the last hour of which necessitated gas and ether anæsthesia. The patient's condition was excellent.

The night following operation she suffered much pain in the right lower extremity, but by the next day this was relieved, and her convalescence was normal.

Four days following operation, we could feel a weak pulsation in the left femoral artery, but in no other vessel of either extremity.

At the end of two weeks the patient was out of bed, a week later walking about with moderate weakness. The tumor was greatly diminished in size, there was no pulsation, thrill or bruit. The woman was feeling well, begging to go home, and finally on the twentieth day following operation, was discharged.

Fourteen months after operation she works hard and says she is well. There is a faint pulse in the left femoral artery at the groin but in no other vessel of either extremity. She declines to return for further treatment. She fears we might want to operate upon her and she might die of the operation (I share with her this fear). We feel that if she lives long enough (escapes some intercurrent disease) she will die of aneurism or of bleeding at the site of ligation.

This is the sixth patient who survived the immediate effects of ligation of the abdominal aorta, and the fourth case that ever left the hospital alive, and did any kind of work.

The cases of Hamann<sup>1</sup> and of Matas<sup>2</sup> remained in the hospital in bed or a chair until they died, one six months, the other seventeen months after operation. Vaughan's case worked twenty-five months and died of large, leaking aneurism. Brooks' case lived three months, and showed at necropsy a large aneurism. Watts' case lived at home for more than three and a half years and died probably of rupture of the aneurism or the aorta.

The data secured through necropsy in the human cases coincide quite accurately with the data secured through experimental work in the laboratory.

Hamann's<sup>1</sup> case presents the only recorded opportunity to note the effect of ligation of the internal iliac artery and aorta in the human being in the absence of any disease of the vessels. At the first operation in April, 1916, the internal iliac artery was tied with chromic catgut. Following this, pulsation ceased for a few days, and in September, 1917, the abdominal aorta just above its bifurcation was tied tightly with heavy silk. Pulsation of the tumor ceased and never returned. On the third day feeble pulsation was felt in both femorals. In the report it was said there was no grossly obvious



gangrene, but on account of pain in the heel and an ulcer on the foot the leg was amputated. There was so little blood in the leg that the amputation stump did not heal. Concerning the collateral circulation, there was evidence of great increase of blood supply over the sacroiliac region around a bleeding bed sore. There were no signs of collateral vessels below the groin. After operation the patient was not improved in any way, and died at the end of six months. At necropsy the aorta at the point of ligation was three-sixteenths of an inch in diameter, and the lumen of the internal iliac was also partially restored.

In Keen's<sup>5</sup> case, reported in 1900, the aorta was completely occluded with four strands of floss silk. Eight days later the femoral pulse was palpable and in two days more pulsation in the aneurism had returned. Forty-eight days after operation necropsy showed the ligature cut through and there was hæmorrhage at the point of ligation and from the sac of the aneurism.\*

Vaughan's<sup>8</sup> case (1920) was of distal ligation of the aorta at a point just below the inferior mesenteric artery; the lumen was completely obliterated at the time of the application of the ligatures. The aneurism appeared to be  $1\frac{1}{2}$  inches in diameter, and of a saccular type, arising from the left side of the aorta, about opposite the origin of the superior mesenteric artery. The pulse of the left foot was felt the day following operation but pulsation was never detected in the vessels of the right extremity. The man worked as a bricklayer and indulged in periodic alcoholic spree until within two weeks before he died.

At necropsy, two years, one month and two days after the operation, the lumen of the aorta and the left common iliac artery had been restored, but the right common iliac was closed by either clot or connective tissue. The aneurism was 7 inches in length, by 6 inches wide (a very great increase in the size over what it appeared to be at the time of operation), the sac filled with firm, laminated clot. There was erosion of the bodies of the second, third and fourth lumbar vertebræ.

Reid<sup>6</sup> in April, 1921, for aneurism of the abdominal aorta just below the renal artery made partial occlusion with cotton tape just proximal to the aneurism; three months later (August 3), he made complete occlusion with cotton tape to the aorta just above the celiac axis. Forty-one days later (September 14), necropsy showed both ligatures had cut through but without hæmorrhage; death was caused by rupture of the aneurism through the diaphragm into the chest. There was no anæmia of the viscera nor infarction of the vessels coming off below the ligature nor any evidence of circulatory disturbance in the lower extremity.

In Matas'<sup>2</sup> case (1925), the aneurism was of the terminal aorta, extending into both iliacs. The aorta was ligated just above the sac, with two completely occluding cotton-tape ligatures, one above the other. Pulsation and bruit in the sac and pulsation of both femoral arteries returned on the

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\* This is the case that caused surgeons to abandon the use of fine ligature material on the aorta.

ninth day. The right femoral pulse disappeared later, the left femoral pulse remained very feeble, no pulse in either foot ever reappeared. The woman had stormy times with many complications and was never as well after as before operation. Frank gangrene did not appear following the operation, but there was a contracture of the right leg, believed to be ischæmic in origin, which became worse following the operation.

Necropsy one year and five months after operation showed that the lumen of the aorta at the point of ligation had been restored to the size of the tip of a uterine probe. The aneurismal sac, though ruptured in several places, was filled with clot, the blood had circulated through the point of ligation into the left common iliac artery, but the right common iliac was obliterated in the walls of the sac.

The case of Brooks<sup>10</sup> was reported in 1926. The artery was ligated in two places, first with a piece of fascia lata and 1 centimetre below this a heavy braided silk ligature. Five weeks later the patient was discharged with pulsation present in the left femoral artery but not in the right femoral nor in the sac. Three months later he died of intestinal obstruction.

At necropsy the obliterated aneurismal sac, the size of a small orange, involved the terminal aorta and both common iliac arteries. The aorta at the site of the silk ligature was constricted. The silk ligature which had cut through lay wholly within the lumen of the vessel enmeshed in a thrombus. The fascia suture had completely disappeared and the aorta at this point was wide open. Both external iliac arteries were open, the right common iliac was partially open, the left common iliac artery and vein were obliterated in the wall of the aneurism. (The left (?) femoral pulse was palpable during life.)

An additional case not previously reported was kindly communicated to me by Dr. Stephen H. Watts,<sup>7</sup> who (1923) made partial obliteration by a tape ligature applied to the aorta just above the sac and below the superior mesenteric artery. The ligature was tightened until pulsation in the sac and femoral vessels was markedly diminished. The lumen of the artery was constricted to less than one-fourth inch in diameter. This patient lived more than three and a half years, with some improvement over her previous condition, and died of what Doctor Watts judged from the description given by her husband to have been rupture of the aneurism.

Of common iliac aneurism, Halsted<sup>8</sup> collected in 1912 all cases reported up to that time. A few are recorded since then. No case has been removed. Eleven cases in Halsted's reports and four or five since then have survived ligation of the common iliac artery. In only two cases were the patients observed for longer than four months, and in one of these, there was recurrence of the signs of aneurism at seven months. Halsted, in one case, applied the completely occluding band to the common iliac artery. Three and one-fourth years after operation, the patient wrote that he was relieved of pulsation and could not feel the tumor through his fat abdomen, but

the leg was cold and so weak and painful he could do little walking. After four or five years more of invalidism he died of undetermined cause.

Thompson<sup>9</sup> records a colorful description of his terrifying experience in dealing with left external iliac aneurism. Six months previously ligation of the left common iliac, followed nine days later by ligation of the right internal iliac, had been done without benefit. To read Thompson's report is discouraging to one who would attempt to do the Antyllus-Matas type of operation for aneurism in vessels beyond the control of a tourniquet.

Aneurism of the innominate artery has never been removed. The vessel has been ligated several times and in the few that survived the operation some temporary benefit but no cure has been attributed to it. The ligature may cut through and cause fatal hæmorrhage in a month.

Many cases of aneurism of the subclavian artery have been operated upon. Only two cases have been removed, both of them by Halsted, and both were cured. No case has been cured by ligation.

Experimental work, especially by Halsted and his pupils and by Matas and others, has brought forth much knowledge of vital importance.

In every case of constriction occlusion of a large artery, in continuity (at a single point without division of the artery), it is proven that regardless of the material employed the lumen of the vessel will be restored, usually within a few days, sometimes weeks. The wall of the vessel at the point of constriction becomes atrophied, new connective tissue forms, in place of the tissue at the point of strangulation, and the ligature cuts through into the lumen. Fine silk ligatures may cut through as early as two days with fatal hæmorrhage. Coarse ligatures are displaced much more slowly, their track becoming filled with new tissue, without the occurrence of secondary hæmorrhage.

Fine ligatures, partially occluding ligatures, and crushing ligatures may work through the wall of the artery before repair and the developing capsule of fibrous tissue are adequate to prevent hæmorrhage.

A metallic band being wider than the ligature, causes atrophy over a larger area of the wall of the vessel, requires a longer time to become thoroughly encased by connective tissue, and consequently entails more liability to secondary hæmorrhage.\* The effects of consecutively placed ligatures close together need further investigation.

Catgut and fascia, tied about the vessel, may loosen, disintegrate and disappear irregularly and too quickly to be safe. This is shown at autopsy in Brooks' case.

The least infection at the site of ligation may be followed by hæmorrhage, extensive thrombosis and gangrene.

To ligate the artery in two separate places, and then cut the vessel between ligatures is the only certain way to prevent restoration of the lumen after

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\* In all cases in which bands had been applied to the human aorta (the last case in 1920), large hæmorrhage or small leakage occurred at the site of necrosis after three weeks. In one case an abscess was formed at the sinus in the vessel wall.

any method of constriction. The work of Brooks, Blalock and Johnson<sup>10</sup> has shown that in the case of the aorta, the immediate mortality and the incidence of gangrene are increased to a percentage making this procedure prohibitive for use in human beings.

For making total non-constrictive occlusion of the aorta in dogs, Reid<sup>11</sup> placed a strip of fascia made in the shape of a sphere into the vessel through a longitudinal incision in the wall of the aorta and sutured it in place by silk. Complete occlusion persisted for six months. It remains to be seen whether this method of dealing with the human aorta will be practical.

Experience and much experimental investigation during the past few years has led to the belief that veins, whether diseased or not should always be occluded whenever an artery is ligated. The investigations of Brooks<sup>12</sup> have contributed some disturbance to this belief. There is one comforting statement, however, in Brooks' conclusions. He would not ligate the companion vein of a large vessel at the time of operation upon the artery, but would reserve vein occlusion until the appearance of some evidence, such as pain, claudication and other signs of ischæmia, and then proceed to ligate the vein. Until it is positively shown that vein occlusion is harmful will it not be wiser to occlude the vein whenever for any purpose an artery must be ligated?

Halsted showed that following ligation of the common iliac gangrene from the operation *per se* is rare. Other factors are of great importance. The only case which was followed sufficiently long to determine the ultimate effects upon the nutrition of the limb is that performed by Halsted himself which after a year showed clinical evidence of ischæmia resulting in almost total crippling of the extremity. This operation was reported in 1912, before the ligation of companion veins was thought of as a useful procedure to be employed when for any purpose large arteries were to be ligated or excised.

For purposes of discussion certain concluding remarks are offered.

The diagnosis of aneurism is not always easy and may be difficult even after the tumor is exposed by operation. Hamann's patient had had one internal iliac artery ligated by one surgeon, and later the abdominal aorta ligated for what was believed when the tumor was exposed, to be aneurism of the common iliac artery, but shown at necropsy to be malignant neoplasm having no connection with the vessel. Diagnostic errors in considering aneurism of the aorta are extremely common—in both directions—and "conducive to clinical humility" (Osler).

In cases of Matas and of Brooks, in which the aneurisms were thought to be of the common iliac, both were shown at necropsy to be of the terminal aorta, and involved the iliacs secondarily. If my case should prove likewise (and such might well be the case), all reported cases of survival after ligation of the aorta for common iliac aneurism will have been cases of error in diagnosis.

Even Halsted mistook for aneurism a case of tortuous subclavian artery; and in another the aneurism believed to be of the innominate, was of the arch of the aorta.

What should be the criteria by which we judge aneurism to be cured? Shall we be deluded into the belief that aneurism has been cured merely because the patient is relieved of pain and pulsation and the size of the tumor is diminished? The dramatic effects of ligation upon the agonizing pain and tumultuous pulsation of the large aneurism might be followed by gratitude so deep as to cause the patient to magnify the amount of relief and minimize the intensity of the still existing symptoms. The surgeon also may be so thrilled with the joy of being able to accomplish the dramatic feat of ligating a large artery and seeing his patient alive the next day that even he may magnify in his own mind the beneficial effects of his accomplishment. After weeks or months have passed, however, coincidentally with the subsidence of the patient's gratitude and the surgeon's initial satisfaction, both individuals may notice symptoms due to return of circulating blood in the aneurism and are then mentally competent to realize the truth concerning the amount of relief secured by the operation.

Sacculated aneurism is a definite gross pathological lesion at the point of the degeneration of an artery and is characterized by progressive increase of size and development of pressure effects upon surrounding structures. The symptoms of aneurism, pain and pulsation, may be temporarily relieved by many remedies, and are subject to spontaneous remissions and exacerbations of intensity. Cases of aneurism have been found at necropsy and even during life in which symptoms were not present or at least not conspicuous. It is an interesting observation that frequently the history of pain and pulsating tumor is of short duration (days or weeks), and there may be found at operation (or necropsy) a sac obviously of much more ancient duration (months). In these cases there are signs of small hole rupture, and leakage of the sac, with secondary sacs and hæmatomata. Might not the age of these secondary formations coincide with the increased pain and size of the tumor?

Can ligation of the artery at any point be expected ever to cure aneurism, or have more than a temporary effect in prevention of further symptoms? Superficial reading of experimental observations, clinical reports and necropsy findings will promptly dispel any such belief. Ligation is essential as a preliminary step before excision or obliteration in aneurisms above the domain of the tourniquet and may be more useful than non-surgical measures in certain cases in which extirpation is not safe, but its function is palliative of symptoms, not curative of the disease. May it not be that the reason gangrene does not more often follow ligation of large arteries is the same reason that the aneurism returns to activity, *i.e.*, the ligated vessel promptly becomes patulous, the blood continues to flow through the same vessels into the aneurism and into the extremity?

The rational and only curative treatment of arterial aneurism is by obliteration or excision of the sac with or without preservation of the artery or restoration of its lumen.

This, since the monumental work of Matas, has been practical in the hands of good surgeons in most cases of aneurism in which the control of the circulation is within the domain of the tourniquet (the extremities).

For aneurisms proximal to the external iliac and terminal portion of the subclavian arteries (without the domain of the tourniquet), no one has yet reported a case cured by the Matas procedure.

Halsted, after ligating from without the sac all vessels communicating with the aneurism, removed the aneurism in three cases; in one from the external iliac artery and in two from the first portion of the left subclavian artery. These are the only cases on record of complete cure of aneurism of any artery between the inner third of the clavicle and Poupart's ligament. No one has reported extirpation of a case of aneurism of the internal iliac, common iliac, aorta, or innominate artery.

This procedure (the Halsted operation) may be performed in one or two stages. It may not be applicable to the aorta above its visceral branches because of the fact that these are located so closely together that they are of necessity involved in all aneurisms of recognizable size and must not be ligated.

The common iliac artery is so short (from  $1\frac{1}{2}$  to  $3\frac{1}{2}$  inches), that excision of a large aneurism of this vessel might entail great danger of having to divide the external and internal iliacs, or the terminal aorta itself.

For these and for all aneurisms of the abdominal aorta does not Reid's successful obturation of the aorta in dogs by a fascial plug sutured in the lumen give hope of successful palliative treatment?

For common iliac aneurism of smaller size, and for all subclavian aneurisms, Halsted's operation can be made safe; and the surgery of arterial aneurism lifted out of the stage of case reports into the stage of organized knowledge.

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# THE RELATION OF THE WELCH BACILLUS TO APPENDICITIS AND ITS COMPLICATIONS\*

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TEN years ago we began a study of the relation of Welch bacillus infection to gangrenous appendicitis and peritonitis and of the possible clinical value of the antitoxin available at that time. In 1923 and again in 1925 we reported our results up to that time which appeared to indicate some value in the use of the serum and suggested the possibility of its usefulness in intestinal obstruction and as a prophylactic in perforating wounds of the bowel and in operations on the intestinal tract.

It may not be out of place to summarize briefly the contents of these previous papers before discussing subsequent experience in this field.

It seemed evident that in gangrenous appendicitis and peritonitis we have to do with a faecal infection due in part, at least, to the activity of the Gram-positive anaërobes that normally infest the gut and whose presence in war wounds was so regularly associated with gas gangrene. We had seen occasionally infection of the abdominal wall after operation for appendicitis in which gas gangrene had supervened and a few similar cases associated with retroperitoneal emphysematous œdema. These cases were unusual. They were all highly toxic in their course and all were fatal. In a few cases we had been led to suspect the presence of the bacillus *aërogenes capsulatus* of Welch and to verify its presence by cultivation and animal inoculation. We considered, at that time, however, that these were rather rare infections. We had no therapeutic measures with which to combat the disease and the difficulties of routine anaërobic bacteriological study hampered further investigation. This was before the war.

There are several things in the picture presented by a case of gas gangrene of the extremities in his last hours that singularly resemble that of one dying of peritonitis. The low temperature, the rapid, feeble pulse, the dusky flush and cyanosis, the dyspnoea, the dilated pupil, the euphoria. The similarity is more than suggestive.

When we returned to civil practice we found one American antitoxin serum—a mixed antitoxin for tetanus and *perfringens*—available, and its use in a series of gas gangrene infections seeming to establish its value, it appeared worth trying in appendicular peritonitis.

I shall not repeat here the résumé of the literature made in 1923. That dealing with the Welch bacillus is massive but discussion of the activity of that organism in surgical conditions within the abdomen is not very rich. I would, however, refer once more to the monograph of Heyde of Friedrich's

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\* Read before the New York Surgical Society, November 12, 1930.

clinic in Marburg, published in 1911 and devoted to a study of the anaërobes in appendicitis. I know of but one subsequent study of equal analytic scope, to which I shall refer later. He attempted to answer the following questions:

- 1.—What anaërobic types are found?
- 2.—How often do they occur?
- 3.—Do particular forms predominate at different stages of appendicitis?

His investigations were painstaking and time consuming. He found that from one to two months were necessary for a complete study of the isolated strains from any given case. His findings are not without interest even now. He found the greatest obstacle to his study in the presence of the *B. coli* which by its rapid growth obscured and distorted the true bacteriologic conditions present. He did not believe that within the animal body the *B. coli* is able to split up proteid with the formation of putrid products but thought that this supposition, which has been so widely held, was due to overlooking the existence of anaërobes which were present at the same time. *Bacillus coli* showed none of that ability to form foul-smelling products credited it by so many authors. He listed seventeen varieties of anaërobes isolated, concluded that anaërobic bacteria were present in one hundred out of one hundred and two cases studied and that they were present in greater profusion than aërobes in all stages of appendicitis and peritonitis and attributed to them the direct causation of inflammation, of gangrene and of toxæmia. He found that the perfringens group—*B. Welchii*—outstripped all others in rapidity of growth.

Simonds, however, in his classical monograph, "Studies on *B. Welchii*, with Special Reference to Classification and to Its Relation to Diarrhœa," noted, in 1915, that the relation of anaërobes in general and of *B. Welchii* in particular to appendicitis was still unsettled. There are, however, some more recent contributions that deserve notice.

Gas bacillus infection of the abdominal wall has been noted and reported by Beer, Winter, Russell, Ochsner, Dayton and others. These spreading gangrenous processes are rare but a milder and comparatively harmless involvement of the fascia and subcutaneous tissue is present in many drained cases. The Welch bacillus can be regularly recovered from such cases by proper anaërobic methods.

Our problem was to study the occurrence of the Welch bacillus from the lumen of the appendix in cases of appendicitis and attempt to evaluate the use of an antitoxin in cases in which we found it in the peritoneal fluid. This we did as follows: We made

1. Anaërobic cultures of the contents of appendices removed at operation.
- 2.—Anaërobic cultures of specimens of tissue taken from the wall without invasion of the lumen of appendices removed at operation.
- 3.—Anaërobic cultures of the fluid removed from cases of peritonitis secondary to gangrenous appendicitis.



- 4.—Anaërobic cultures of the blood in cases of proven *B. Welchii* peritonitis.
- 5.—Post-mortem studies in cases of death due to peritonitis and appendicitis.
- 6.—Clinical studies of the value of antitoxin in cases proved by culture to be infections with *B. Welchii*.

We found that cultures made from the contents of the lumen of appendices removed at operation showed the presence of *B. Welchii* in 90 per cent. of the cases.

In seven cases in which the appendix was acutely inflamed, thickened and œdematous but with no gross perforation, cultures made of portions aseptically removed in the operating room and so cut as to remove the peritoneal and muscular coats of the organ without invading its lumen also showed the presence of *Bacillus Welchii*.

In sixteen cases, localized pus collections with gangrene showed *B. Welchii* and in forty cases in which culture was made from free fluid in the pelvis or general peritoneal cavity, *B. Welchii* was found ten times.

The results of blood culture were, for the most part, negative. The studies of the blood made in cases of gas gangrene during the war showed that blood culture is negative at the beginning of gangrene. In cases fully developed Lardenois and Baumel found seven positive cases in forty-eight cultures. Weinberg and Segine found four positive cultures before death in twenty cases of hæmoculture. Delbet and Fiessinger found two positive in seven blood cultures made in the agonal period. It is evidently the general opinion that the passage of organisms into the blood occurs just before or after death as the antitryptic indexes alkalinity are lowered.

It seemed to us evident that the Welch bacillus was present in the lumen of most appendices and is frequently found outside of the gut in an actively growing form in appendicular abscess and in localized peritonitis and in a rather large number of cases in free peritoneal exudate, that in most cases its activity is cut short by operation with removal of the appendix but that this is not always the case and it is apparently an active factor, if not the most active factor, in the production of a fatal disease.

In the beginning of the work we were handicapped by the fact that culture made at the time of operation required from twelve to twenty-four hours for an available report. We found, however, that by making injections of the suspected material in the liver of the living guinea pig, killing the animal at the end of three minutes after injection, and placing the animal in the incubator, study of the liver, at the end of two hours, was an adequate clinical test. Smears were taken from the bloody peritoneal fluid, the liver itself and from the heart's blood. In positive cases the organism could be seen easily. According to our records there were 97 per cent. positive findings in animals after two hours compared with the positive anaërobic milk cultures. We felt, at that time, the desirability of an assured bacteriological diagnosis before ad-

ministering the antitoxin. It was, and is, expensive. The reactions when given by the intravenous route were quite severe and sometimes alarming and we were feeling our way. After using this routine for about four years we thought we could recognize, in the clinical appearance of the peritoneal exudate and by the examination of smears made at the table, the presence of the Welch bacillus sufficiently accurately for our purpose and described the cases thus.

The cases of diffuse peritonitis in which the anaërobes are present in numbers show a more or less typical clinical picture. The temperature is not, as a rule, much elevated, the pulse rate out of ratio, they are cyanotic and the pupil is dilated, a dusky flush may be present. At section the fluid may be foul or not, a dark colored or coffee-ground fluid is sometimes seen. One may find, in the region of the base of the cæcum, an emphysematous retroperitoneal cellulitis spreading and sometimes extending to the anterior abdominal wall. The progress of such a case may be quite favorable for from twenty-four to forty-eight hours when with comparatively little distention and little or no regurgitant vomiting the pulse becomes rapid and thready, cyanosis becomes more profound, the skin grows clammy, respiration more and more rapid and death occurs.

We then gave up the guinea-pig culture method which we felt we could do without but did not begin routine prophylactic injection until several cases of gangrene of the appendix with but slight peritoneal involvement apparent at the time of operation unexpectedly developed peritonitis on the third or fourth day, which went on to a fatal termination with the proven presence of Welch bacillus, missed by smears at the table and unsuspected. We had been considering the path of infection from the lumen of the appendix into and through its wall to the peritoneal cavity eventually, terminally, or post-mortem to the blood-stream. It had not occurred to us that after the removal of the appendix any large infected area of bowel wall might remain in the picture.

The following case was enlightening:

CASE 729.22, a child of five years, showed a general diffuse peritonitis of seventy-three hours' duration with cyanosis, distension, feeble and thready pulse. At operation, free turbid fluid in the peritoneal cavity; a leaking abscess. Appendix showed terminal gangrene with a small perforation. One hundred cubic centimetres of perfringens antitoxin were given on the operating table; six hours after operation the radial pulse was imperceptible and more serum was given, 150 cubic centimetres in the vein, 200 cubic centimetres in the axilla, following which the little patient rallied a few hours; later another collapse was controlled by more serum. Altogether 970 cubic centimetres of serum were given, most of it intravenously. The patient rallied after each administration. Seven days after operation lobar pneumonia developed. In the meantime the abdominal distension continued extreme and never yielded to treatment. On the eleventh day the pulse became imperceptible, the skin cold and clammy, and she died. The cultures were positive for *B. Welchii*. At autopsy the last 12 inches of ileum were found gangrenous and adherent to the pelvic wall. The intestine above it was greatly distended—a complete obstruction. The general peritonitis had subsided but the local gangrenous process in the terminal ileum had gone on.

It was apparent, in this case, that the antitoxin had been sufficiently active to control the toxæmia of the peritoneal infection but that the local gangrenous process in the terminal ileum had produced an intestinal obstruction which proved fatal. We then observed particularly the condition of the terminal ileum in autopsies made on cases dying of gangrenous peritonitis and found in most of them a much thickened wall with diffuse hæmorrhagic ulceration and beginning gangrene. It was evident that this portion of the bowel was paralyzed by an inflammation approaching gangrene and would act at once as a passively obstructed segment and a source of absorption of toxic matter. This suggested inspection of the terminal ileum in cases in which this seemed safe at operation and we were interested to find, in practically every case, a greater or less degree, in many cases marked, of œdema, thickening and loss of peristaltic excitability.

It seems probable that many cases of so-called acute appendicitis are in reality acute inflammations of the terminal ileum and cæcum in which the appendix, on account of its terminal blood supply, offers less resistance than the other lymphoid structures. How important a factor this ileo-typhilitis is in the mortality of appendicitis our autopsy material does not allow us to infer, but it would seem to be not entirely negligible.

Williams made a therapeutic test of the value of *Bacillus Welchii* antitoxin in cases of general peritonitis and intestinal obstruction at St. Thomas' Hospital. Antitoxin was given to eighteen of the most severely ill of a series of 256 consecutive cases of appendicitis with a reduction of mortality from 6.3 per cent. in a parallel series to 1.17 per cent. His conclusions were: In cases of peritonitis with paralytic obstruction there was a marked clinical improvement as the result of administration of *Bacillus Welchii* antitoxin. In cases of organic obstruction similar effects were obtained but in individual cases it was as a rule impossible to differentiate between the effects of the serum and the effect of successful operative relief of obstruction.

Williams, however, reported no bacteriologic studies of appendices or of peritoneal exudate and his work was based on the assumption that death, in septic peritonitis, is the result of absorption from the paralyzed small intestine of the toxins of the *Welch* bacillus. His use of the antitoxin was directed to the neutralization of this poison. He does not discuss any intoxication save that from within the gut.

Copher, Stone and Hildreth made an experimental study of the value of antitoxin in intestinal obstruction and peritonitis in dogs. They report that life was prolonged in the experimental series of dogs having acute, general peritonitis and acute intestinal obstruction by the use of the *B. Welchii* antitoxin.

Bower and Clark reported the use of *B. Welchii* antitoxin at the Samaritan Hospital in Philadelphia. In eleven cases of acute diffuse suppurative peritonitis, nine cases of acute intestinal obstruction and five cases of acute suppurative cholecystitis, they were convinced of its value.

Morton and Stabins studied experimentally the effect of *B. Welchii* antitoxin in high intestinal obstruction in dogs. They conclude that their results support the contention that the toxin of *B. Welchii* has a bearing on the toxæmia of intestinal obstruction. In a large number of cases the antitoxin of the *B. Welchii* seems to be potent in combination with surgical procedures to relieve the obstruction in bringing about the recovery of dogs with obstruction—control dogs do not recover under similar circumstances.

## WELCH BACILLUS AND APPENDICITIS

With regard to the use of Welch antitoxin in intestinal obstruction we have been disappointed. In several cases, remarkable but relief improvement has followed the administration of larger doses; in a few its use has apparently contributed to recovery. In most of the cases in which it has been used its value did not appear. It is in France, however, that the most advanced work has been done.

Michel credits to Paul Delbet at the suggestion of Weinberg the first employment of anti-gangrene serum in appendicitis. He reported thirteen cases at the twenty-ninth Congrès Français de Chirurgie with twelve recoveries.

Bérard and Cotte later reported nineteen cases with sixteen recoveries.

Bouchez in his Thèse de Paris, 1920, discussed the use of anti-gangrene serum in infections of intestinal origin with successful animal experimentation.

Michel and his pupil Rakovatz report that serotherapy and surgery show a mortality of 15 per cent. in cases which he charges with an expected mortality of 70 per cent. treated by surgery alone.

Weinberg, Prévôt, Davesne and Renard present studies on the bacteriology and the sero-therapy of acute appendicitis—a most complete and satisfying investigation which should be read entire.

They conclude that work on the bacteriology of appendicitis may be divided into three epochs. In the first, the isolation of aërobic organisms; in the second, beginning with Vuillon and his collaborators the primordial rôle in the evolution of that infection was attributed to the anaërobes neglecting or relegating to a second place the aërobic organisms. In the third, in which they now struggle, the ideal is to assign to each germ in the often very complex flora of a given case the part played by it in the symbiosis. They describe many combinations but consider that the primordial rôle in appendicitis belongs to *B. coli* and *B. perfringens*. They advise the use of a mixed serum to which anti-*coli* serum is added. They are better provided with antigangrene sera than we are but it is evident that they consider the perfringens antitoxin as the most valuable constituent of them all. They advise, as does Michel, the delay of surgical intervention in advanced cases until the administration of antitoxin has had time to take effect. They go so far as to suggest its use in the medical treatment of early cases.

*Antitoxin.*—In the beginning of our work we gave antitoxin intravenously with severe reactions in many cases in spite of subcutaneous injection of small amounts of serum given an hour before for desensitization. Increasing subcutaneous doses were then used over several hours for the same purpose. A measure of success followed this procedure but reactions, some quite severe, continued to occur. A few were alarming and for the last five or six years we have found just as satisfactory results with the subcutaneous method. We now adopt the following routine:

In all cases in which gangrenous change is apparent in the appendix 100 cubic centimetres of antitoxin is added to 1000 cubic centimetres of normal salt solution and given by hypodermoclysis. Anaërobic and aërobic cultures are made from the peritoneal exudate in the immediate neighborhood and from the fluid found in the pelvis, and further administration of antitoxin is guided by the result of culture and by the course of the case. If the organism is present in the peritoneal fluid and if evidence of peritonitis appears, and especially if the patient shows a rapid pulse with cyanosis, repeated and larger doses are administered—200 cubic centimetres daily for two or three days. The immediate effect of the antitoxin is more dramatic when given by the vein, but its action, while slower, is more prolonged by

the subcutaneous method, with no reactions. From five to ten days after injection serum rashes regularly appear.

The actual value of such a method of treatment can be determined only by an extended use in routine by a number of men in several institutions. I have used it with some freedom in more than one but have thought it best to present fifty cases from one hospital and to compare this series with the mortality of a larger group.

In a series of 450 cases of acute appendicitis cared for by several operators at the Brooklyn Hospital in the last five years, 297 were suppurative or catarrhal; of these two died, a mortality of .67 per cent. One hundred fifty-three cases were gangrenous with more or less peritoneal involvement. Of these twenty-five died—a mortality of 16 per cent. Of this group ninety-eight were cases of localized gangrene or abscess, of which thirteen died, thirty-eight were classed as spreading peritonitis with six deaths, and seventeen as generalized peritonitis with six deaths.

In the group treated with antitoxin there were no simple or suppurative cases. The serum was used only in cases of gangrene and its sequelæ, often late, often sparingly.

There were, however, ten cases of localized gangrene and abscess with one death, fifteen cases of spreading peritonitis with three deaths and twenty-five cases of general peritonitis with six deaths.

In the first series, the deaths from general peritonitis showed a 35 per cent. mortality; in the second (with antitoxin), a rate of 24 per cent.

It will require a much larger series and a more consistent use of antitoxin early, before a true estimate of its value can be made. At present it is our feeling that it should be tried in all cases presenting gangrenous change in the appendix at operation and in cases showing evidence of any peritoneal involvement at that time, and that its use should be extended until the case is out of danger or beyond help. A more critical and complete bacteriological study of appendicitis and of intestinal sepsis and a clinical evaluation of its results are most evidently needed and a larger *materia medica* of antitoxin sera would seem from the French experience to be needed. It is to be hoped that both these needs may be supplied.

#### ILLUSTRATIVE CASES

CASE I.—W. D., Jr., a boy of ten years, who had been sick for a week, was admitted with a rigid and somewhat distended abdomen with a tender mass in the right iliac fossa. Cyanotic, dilated pupils. Temperature 102°, pulse 140, respirations 40. Operation showed a generalized purulent peritonitis, a gangrenous appendix hanging over the pelvic brim, which contained foul, brown fluid. Appendectomy and drainage. Antitoxin immediately—100 cubic centimetres by clysis, repeated once on the second day. Pulse reached normal on the third day, temperature, on the sixth, after which a good recovery. Culture—B. Welchii and colon.

CASE II.—D. J., a child of eight years, admitted after two weeks of fever with a mass in the right lower quadrant size of a grapefruit. Temperature 104°, pulse 140, respirations 40. Operation showed an appendicular abscess which contained about 3 ounces of foul pus. There was some spreading peritonitis present. Antitoxin, 100

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cubic centimetres, was given on the day before operation by clysis and this was repeated two days later. The cyanosis did not disappear until after the second injection. A moderately stormy convalescence was established by the seventh day.

Note the early subcutaneous use of serum.

CASE III.—S. S., aged forty-five years, admitted forty-eight hours after the beginning of her third attack. Her pain began in the right lower quadrant which persisted in spite of castor oil and enemas, and at the time of admission to the hospital was general. She vomited thirty-eight hours after the beginning of the attack. Her abdomen was moderately distended and generally tender, the right side more than the left. Her entire right side was markedly rigid. There was moderate rigidity on the left side, more marked below. Her temperature was  $102^{\circ}$ , her pulse 120, her respiration 40; 17,000 leucocytes, 8,070 polymorphonuclears. She was somewhat cyanotic. She was operated on immediately and a gangrenous appendicitis with general peritonitis, foul, free pus, creamy brown, foul, surrounded the purple and inflamed coils of small intestines. The pelvis was full of foul pus; there was more pus in the right kidney fossa.

An appendectomy was performed and a drain inserted to the pelvis and to the appendix stump. She received 100 cubic centimetres of perfringens antitoxin intravenously on the second day and another 100 cubic centimetres by clysis on the third. Her convalescence was stormy with repeated vomiting, approaching faecal in character, a low temperature and a high pulse rate, which reached ninety on the seventh day, after which she made an uninterrupted recovery. Culture of the peritoneal fluid gave *B. Welchii* in pure culture.

CASE IV.—D. P., admitted with a history of vomiting and abdominal pain for twelve days; the pain in the main, suprapubic. Temperature  $100^{\circ}$ , pulse 100, respirations 20; leucocytes 14,400, polymorphonuclears 82 per cent. A large, rounded mid-line mass between the navel and the pubes. Operation showed the whole lower abdomen filled by an inflammatory mass; finger dissection, after walling off, opened a cavity containing about a quart of foul-smelling, thin pus. A counter incision and drain in left inguinal region and rubber tube drains to the cavity in the pelvis. No attempt to find the appendix. A faecal concretion was found in the cavity. He did not receive any antitoxin until the first day after operation when he was given 500 cubic centimetres in the vein. This was repeated in the next two days until he had 1,000 cubic centimetres in all. A temporary improvement was not maintained. An overwhelming intoxication carried him off by death on the fifth day.

CASE V.—F. R., a girl aged sixteen years. Pain in the epigastrium two days before admission; vomited repeatedly the next day and pain shifted to the right lower quadrant. On admission, marked right-sided rigidity, most pronounced below. Rectal examination revealed a mass in the right upper pelvis, very tender to touch. Temperature  $100.2^{\circ}$ , pulse 160, respirations 40; leucocytes 23,600, 90 polymorphonuclears.

At operation four ounces of opaque yellow fluid escaped. The omentum fastened to the base of the caecum from which an appendix,  $3\frac{1}{2}$  inches long, ran straight down from the brim to the bottom of the pelvis. The distal half was gangrenous and perforated with free faecal matter surrounding it. The appendix was removed and a  $\frac{5}{8}$ -inch tube with raffia to the bottom of the pelvis, a smaller soft tube to the base of the caecum.

One hundred cubic centimetres *B. Welchii* antitoxin was given eighteen hours after operation and repeated every twelve hours until 600 cubic centimetres had been given. The pulse rate fell to 100 on the second day and remained there. The temperature reached normal on the eleventh day. She suffered from marked distention and vomited faecaloid material on the third and fourth days. Lavage was not needed after the fifth and she made an uncomplicated recovery.

Culture *B. Welchii* and colon bacillus.

The faecal peritonitis, the immediate response of the pulse rate to antitoxin, the continued fever and peritonitis, the critical period of the fourth and fifth days and the associated colon infection are noted.

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## POST-OPERATIVE PAROTITIS\*

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ALTHOUGH this condition was first described by Munde in 1878 following ovariectomy, Paget as early as 1886 reported 101 cases of secondary parotitis, one-half (fifty-one) of which took place after operation upon the abdomen, which included gastrotomy, enterostomy, as well as herniotomy, colostomy, abdominal and umbilical tumors and penetrating wounds of the abdomen. The other 50 per cent. occurred after operations upon the female genitalia. He declared that the peritoneum, genital organs and parotids were indirectly and reflexly related (bear in mind that abdominal surgery then chiefly dealt with the pelvic organs, particularly with ovariectomy). In 1889 Hanau stated that parotitis occurred secondary to infection of Stenson's duct by mouth organisms. However, the two theories, namely that metastatic foci develop in the gland only from sepsis on the one hand and that it is a local extension of infection from the mouth up Stenson's duct on the other, have continued until today, the more general consensus on opinion favoring the later view. Hanau and Pilliet believe that the organisms go up the duct and in their pathologic specimens demonstrated that the inflammation began around the ducts and spread outward into the perilobular tissue, whereas, they argued, should the etiology be embolic the inflammation should at first appear as a perivascular process. The outer one-third of the duct contains the same organisms as found in the mouth.

A close analogy is suggested between infections of the salivary glands and other large glands which also empty into mucus-lined cavities. The cases usually fall into two broad groups, one in which an acute inflammation of the gland is the first noticed and predominant symptom, and the other presenting primarily recurrent symptoms of duct obstruction. Added to the obstruction there may be any grade of inflammation of the gland and duct. The obstructing agent might be simply the swelling and thickening of the mucosa or a plug of mucus lodged at the meatus or some inflammatory constriction or a stone formed anywhere in the duct. While it is now generally accepted that at least the great majority of pyogenic inflammations of the parotid gland are due to an ascending infection there is evidence to warrant the belief that a blood-born infection is an occasional cause of acute suppurative parotitis. It is also likely that infection may be born by the lymphatic channels.

In addition to the presence of oral infection the most commonly mentioned predisposing factor is dryness of the mouth following operation, due to the

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practice of withholding fluids as well as the temporary hyposecretion following hypersecretion during and after narcosis. In this connection it is interesting to note the report of the study of 1,000 cases of gastric ulcer treated medically and not surgically. In 470 cases treated with oral starvation there were twenty-one cases of parotitis, an incidence of 4.5 per cent., while in 530 cases allowed something by mouth there were only two cases of parotitis, an incidence of but 0.4 per cent. It is apparent from these figures that acute suppurative parotitis occurs ten and one-half times more frequently in such cases of gastric ulcer than in cases allowed fluids by mouth. In this series mouth washes did not seem to have any influence upon its occurrence. Of course the question naturally arises that if dryness of the mouth is an exciting factor why do not the sublingual and submaxillary glands become involved, although they very rarely do. This is explained by Lynn on the basis that the parotid is essentially a serous gland while the submaxillary and the sublingual are of the mucous variety. Stuart Low has demonstrated a definite inhibitory effect of mucin on bacterial growth. Likewise the parotid contains lymph nodes while the other glands do not, thus favoring the extension of inflammatory processes. On the other hand Buscarlet and Kaiser abroad and Jennings and Fisher in this country hold the view that secondary pyogenic parotitis originates as a result of metastatic foci from purulent exudate elsewhere in the body or as a part of a general pyæmia. As a rule the evidence of positive blood culture is lacking. The supporters of the hæmatogenous theory believe that the infected emboli find favorable soil in the parotid gland as the masseter muscle interferes with the blood supply to the gland and congestion often develops. Against this theory is the fact that it may occur in cases where the operative wound healed by primary intention with an entirely aseptic course. I believe that it has been clearly demonstrated that the type of anæsthetic or the preliminary hypodermic have no bearing.

Traumatism at the time of operation, by pressure upon the angle of the jaw and the gland has been mentioned by some authors but I believe that the occurrence is as great in cases operated under other types of anæsthetics than general (local and spinal) or in cases where particular attention has been paid to this as a causative factor.

*Occurrence.*—The condition occurs most frequently in adults, especially after the third decade of life. It is more common in the female; this I believe is due to the fact that the majority of abdominal operations are upon the female. More cases have been noted to occur from November to April when respiratory infections are more prevalent; 20 to 33 per cent. are bilateral. Most cases follow severely infected conditions, appendicitis, peritonitis, perforating gastric ulcer, and so forth. In fact, next to ovarian cyst, perforating gastric ulcer is said to be the most frequent operative condition which is followed by parotitis. Collins reports 6,100 operative cases with eight cases of parotitis, 0.13 per cent. (one of these occurred awaiting operation). All these cases were abdominal operations. This series now includes

thirteen cases occurring in 2,716 major operations (0.47 per cent.). There were four deaths and nine recoveries, and two cases were not operated upon.

*Classification.*—Deaver prefers to classify these cases as follows: 1, Metastatic, in pyæmic conditions; 2, ascending, *via* the ducts; 3, traumatic. I believe that a better classification and one that is more helpful in indicating the treatment is as follows: 1, Simple acute; 2, acute suppurative; 3, gangrenous.

*Bacteriology.*—The most common infecting organism is the staphylococcus. The other organisms that are found are the pneumococcus, streptococcus, and bacillus coli in the order named. Hellendale reports one case of post-operative gonorrhœal parotitis but he does not think that the demonstration of gonococcus pus from the parotid is any final proof of the hæmatogenous origin of the infection.

*Signs and Symptoms.*—The condition usually appears in two to ten days following operation, although Fowler reports one case eighteen days post-operative. There may be no great change in the patient's general condition while on the other hand there is usually a sharp rise in the patient's temperature, even to 104° F. or 105° F., with a corresponding increase in the pulse rate. The attack is ushered in, as a rule, by severe pain in the region of the angle of the jaw. The pain is severe owing to the abundant strong fibrous septa throughout the gland which is of the racemous type, thereby permitting very little tension. The location and relation of the gland is also a factor in the production of pain. Swelling of the glenoid portion of the gland produces pain in the ear and in the temporo-maxillary articulation. Swelling of the carotid and pterygoid lobes causes pain and fulness in the throat. Opening the jaw decreases the space between the jaw and the external auditory canal and mastoid, thereby pinching the gland. Dyspnœa and dysphagia may be evident due to pressure inward of the swelling. While extension from one lobe to another is slow due to the dense septa the whole gland is often involved in the process.

*Clinical Course.*—This may be mild with little fever and slight discomfort or moderate pain and slight swelling limited to the parotid region. On the other hand the conditions may be extremely severe from the first with all the clinical symptoms and laboratory findings of a severe infection, including great pain in the gland, chills, high fever and marked swelling, first in the gland itself and then later a rapidly spreading œdema of the neck, head, and face. This œdema may close the eyes and may involve the neck down to the clavicle. It may extend inward into the pharynx embarrassing the air passages. Delirium may intervene and in children there may be convulsions. The process may rupture into the external auditory canal. Seventh nerve involvement is rare. The process may rapidly become gangrenous.

*Diagnosis.*—This is based upon the history of a recent injury or operation, discomfort and pain in the neck, swelling and tenderness of the gland and constitutional and laboratory findings of a pyogenic infection. If the operative field is nearby a differential diagnosis of a lymphadenitis or cellulitis must be made. The constitutional symptoms depend upon the severity of

the infection and the reactionary power of the patient. The temperature may be  $103^{\circ}$  F. to  $105^{\circ}$  F. and the pulse 110 to 130. In cases of low virulence the temperature may only reach  $99^{\circ}$  to  $99.5^{\circ}$  F. The leucocyte count varies from 9,000 to 25,000. In seeking parotid tenderness and swelling bear in mind the gland runs forward below the lower border of the zygoma and extends backward behind the ramus of the jaw below the lobe of the ear.

*Prognosis.*—Every post-operative parotitis is a potential lethal factor until it proves itself benign, and to await spontaneous evolution jeopardizes life. The death rate is 33-33.5 per cent. in those cases requiring incision and as high as 42.8 per cent. in all cases. This figure may be inaccurate by the fact that the original condition for which operation is performed is often a definite factor in the mortality. In the cases in which the parotid infection was but one evidence of a terminal condition it is an essentially fatal malady and not favorably influenced by any form of treatment.

*Complications.*—These need only be mentioned and may consist in thrombosis, phlebitis, or ulceration of large vessels with hæmorrhage necessitating the ligation of the external carotid. Sinus thrombosis, meningitis, retropharyngeal abscess and abscess of the mediastinum are to be thought of.

*Treatment.*—A differential diagnosis of the type suggests at once the method of treatment. This condition is a comparatively infrequent complication of operative surgery and for this reason the experience of the average surgeon in its treatment is necessarily limited. The lightning-like rapidity with which it attacks the patient already severely handicapped often overwhelms both the patient and the attendant. The treatment may be divided into the prophylactic and the active. Prophylactic treatment should consist of the following measures: careful manipulation of the patient's jaw by the anæsthetist to avoid trauma to the gland. A rigid and careful mouth toilet of every patient prior to anæsthesia. Any infection of the gums should be painted with tincture of iodine. Dryness of the mouth should be prevented after operation. This can be best accomplished by supplying fluids liberally to the patient either by rectum or by hypodermoclysis. The needles for giving fluids by hypodermoclysis can be left with safety in the patient for four or five days and a pint of fluid given every three or four hours, thus avoiding the pain and discomfort of reinserting the needles each time. The patient may be allowed to suck ice or better still lemon stick candy, the acid of the lemon stimulating the salivary secretion.

A case of parotitis having developed, it is quite essential that we early determine the type with which we are dealing. If the simple acute, the application of either ice bags to the gland or hot fomentations will suffice. Opinion differs as to which is the better. The application of an ointment of belladonna and ichthyol to the parotid region which is covered with oiled silk and then hot fomentations seems to give relief to a certain extent. Alpine light therapy may be of benefit.

If possible to open the mouth one should see that the duct is open by

manipulation or probing. If obstruction is met with assure yourself by palpation or X-ray that stone is not present. Patency of the duct must be maintained if possible by probing or splitting the opening of the duct. Operation for drainage of the gland becomes imperative as soon as it appears probable that the gland infection is not going to subside spontaneously or in those cases in which we are dealing with an acute suppurative type from the start as evidenced by the clinical picture. Owing to the toughness of the capsule it is difficult to demonstrate fluctuation. Doubtful cases should be drained not later than forty-eight hours from the onset to avoid suppuration and gangrene, as well as possible rupture into the throat or external auditory canal. Where necrosis has occurred the convalescence will be slow and one has a long-continued, tedious, painful dressing case. Continuous moist heat is valuable at this stage.

The method of incision of Lilienthal I believe to be the safest and best. This consists of a vertical skin-deep incision extending from in front of the auricle and just as close to it as possible. The incision is extended to the hollow behind the angle of the jaw and thence in a gentle curve forward as far as the projection of the anterior border of the masseter muscle. The flap of skin thus formed is reflected forward revealing the greater part of the parotid gland with its overlying fat and fascia. Incisions, as many as appear necessary, may now be made through the parotid fascia into the gland itself the line radiating in a general way along the course of the pes anserinus. No incision, however, should cross the line of Stenson's duct. Deeper collections of pus may be evacuated through the same cutaneous incision by puncturing through the fascia behind the ramus of the jaw and then enlarging the opening with a director or dressing forceps.

CASE REPORTS.—CASE I.—Male, aged thirty-six, admitted June 5, 1928, streptococcic cellulitis of left leg complicated by acute nephritis and diabetes mellitus; incision and drainage. On nineteenth hospital day, swelling of left parotid gland noted with severe pain and difficulty in swallowing. At end of forty-eight hours, incision, no pus, followed by subsidence of swelling. After four days, swelling and tenderness of right parotid gland developed which, under heat, subsided after three days. Patient died thirty-eight days after original admission.

CASE II.—Male, aged forty, admitted June 20, 1928; severe general abdominal pain; no localization at any time; stools fluid and frequent; abdomen distended from tympanites; temperature normal; pain subsided end of fourth day; simultaneously (tenth day of illness) developed sharp pain and swelling in right parotid region; elevation of temperature to  $103.2^{\circ}$ ; incision of gland evacuated large amount of pus, drainage; forty-eight hours later, right peritonsillar abscess opened and drained, spontaneous escape of pus through right external auditory canal; from this point, uneventful convalescence.

CASE III.—Woman, aged twenty-five, admitted July 7, 1928; salpingectomy and appendectomy; morning of second post-operative day pain with moderate swelling and tenderness over both parotids; iced fomentations for one day, then changed to hot fomentations; relief after forty-eight hours; four days from onset swelling and pain had disappeared; temperature normal.

CASE IV.—Woman, aged twenty, admitted March 11, 1928; hysterectomy and appendectomy; forty-eight hours after operation, right parotid swollen and tender; oil of wintergreen applications over gland with little relief; fourth day heat applied; sixth day

local condition aggravated, condition stationary for four days; twelfth day right side of face and neck greatly swollen, no pain; Alpine light applied, heat continued, temperature normal.

CASE V.—Man, aged sixty-six, admitted May 22, 1928; cancer of rectum; preliminary colostomy; removal of rectum by transsacral route; eleventh post-operative day left parotid gland swollen and tender; general failure with death fourteen days post-operative.

CASE VI.—Woman, aged twenty-three, admitted November 22, 1926; bilateral salpingectomy and appendectomy; morning of day after operation, parotid gland swollen and tender, ice bags, gradual subsidence of pain and swelling with both glands normal by fifth day post-operative.

CASE VII.—Woman, aged thirty-one, admitted January 24, 1927; cholecystectomy and appendectomy three years previously; now admitted because of pain throughout abdomen; abdominal distention and tenderness; no operative interference; gradual improvement in abdominal pain and tenderness. On third day, swelling and tenderness in right parotid region; ice bag applied; increase of local pain; fifth day entire right side of face and neck, including right eye, swollen and tender but not very painful; belladonna ointment; seventh day temperature normal, swelling subsiding, recovery.

CASE VIII.—Man, aged forty-nine, admitted May 28, 1928, ruptured appendix, general peritonitis, appendectomy, multiple drainage. Hypodermoclysis normal salt solution each day post-operative; fourth day pain and tenderness left parotid region; parotid gland swollen; fifth day pain and tenderness and swelling in right parotid gland; ice bags; pain and swelling in both glands gradually subsiding and by tenth day condition had entirely subsided.

CASE IX.—Woman, twenty-one years, admitted April 3, 1927, appendectomy for chronic appendicitis; second day post-operative swelling and tenderness in right parotid region; rapid swelling and pain in gland and face; dry heat applied; following morning marked increase in symptoms; ichthyol and belladonna ointment applied with dry heat; following day dry heat discontinued, hot moist packs applied; by sixth day swelling and pain greatly decreased, temperature normal; uneventful recovery.

CASE X.—Boy, aged thirteen, acute suppurative appendicitis; appendectomy with drainage; uneventful course for eight days; on eighth day developed pain and swelling in right parotid gland; gland became quite swollen and painful; temperature elevated for five days; gradually dropped, reaching normal on fourteenth day post-operative with subsidence of swelling and disappearance of pain; recovery.

CASE XI.—Man, aged sixty, admitted December 9, 1925; acute gangrenous appendicitis; appendectomy with multiple drainage; diffuse peritonitis; tenth day post-operative marked swelling of left parotid gland with pain; thirteenth day swelling of gland had diminished; general condition bad; death of patient.

CASE XII.—Girl, aged nine, admitted August 14, 1929, acute gangrenous appendicitis; appendectomy, drainage; on twentieth day post-operative after apparent normal wound course pain and tenderness developed in region of right parotid gland; questionable whether the condition was one of mumps or was a mild post-operative parotitis; after two days left side of face was œdematous, slightly tender with normal temperature, pulse and respiration; from this point on the convalescence was uncomplicated.

CASE XIII.—Man, nineteen years, fracture of ribs and vertebræ, traumatic; laminectomy. Three days post-operative right parotitis developed; following day this was bilateral; general condition of patient bad; patient died five days after operation.

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# BLEEDING GASTRIC AND DUODENAL ULCERS\*

REPORT OF 52 CASES

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IN DISCUSSING bleeding ulcers, confusion may arise unless one definitely states to which type of case one is referring. This presentation will include only those cases that have had one or more gross hæmorrhages that were severe enough to confine the patients to the hospital. Cases in which an occasional tarry stool has occurred, or those in which occult blood has been found in the gastric or stool examination, are excluded. During the past nineteen and one-half years, or from January 1, 1911, to July 1, 1930, there have occurred fifty-two cases of bleeding ulcers in the Fourth Surgical Division at Bellevue Hospital. These cases have been divided according to the year of hæmorrhage to determine whether there has been an increase in the frequency during recent years, and Table I will reveal a marked increase

TABLE I  
*Year in Which Hæmorrhage Occurred*

|            |   |             |    |
|------------|---|-------------|----|
| 1911 ..... | 4 | 1922 .....  | 0  |
| 1912 ..... | 1 | 1923 .....  | 1  |
| 1913 ..... | 2 | 1924 .....  | 3  |
| 1914 ..... | 1 | 1925 .....  | 2  |
| 1915 ..... | 1 | 1926 .....  | 2  |
| 1916 ..... | 1 | 1927 .....  | 3  |
| 1917 ..... | 0 | 1928 .....  | 10 |
| 1918 ..... | 1 | 1929 .....  | 13 |
| 1919 ..... | 0 | 1930 .....  | 6  |
| 1920 ..... | 0 |             | —  |
| 1921 ..... | 1 | Total ..... | 52 |

during the past two and one-half years. During this period twenty-nine hæmorrhages occurred, or over 50 per cent. of the total. A paper<sup>2</sup> on acute perforated ulcers, which included 105 cases from the Fourth Surgical Division from 1911 to 1929, revealed one perforation in 1911 as against thirteen for 1929. Whether this increase in complications is due to more conservative treatment of ulcers during the past few years I would not attempt to say, but Eusterman, in discussing a recent paper of Balfour's<sup>1</sup> in which 500 consecutive cases of duodenal ulcer were studied in which gastroenterostomy alone was done during the years of 1918 and 1919, stated: "The fact that 87 per cent. of patients with duodenal ulcer had complete cure or satisfactory relief is a commendable showing. That such cases are safeguarded from

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future perforation and to a large degree from further hæmorrhage and that subsequent disturbances are easily controlled is worthy of note."

The cases with which we are here concerned have been divided according to the month in which the hæmorrhage occurred, and in Table II it will be

TABLE II

*Month in Which Hæmorrhage Occurred*

|                |    |                 |    |
|----------------|----|-----------------|----|
| January .....  | 5  | August .....    | 4  |
| February ..... | 11 | September ..... | 4  |
| March .....    | 4  | October .....   | 3  |
| April .....    | 5  | November .....  | 2  |
| May .....      | 6  | December .....  | 4  |
| June .....     | 2  |                 | —  |
| July .....     | 2  | Total .....     | 52 |

noted that eleven cases, or one-fifth of the total number, occurred in February. It was thought advisable to further divide the cases into three groups: Group I, cases that died with or without operation; Group II, cases not followed since leaving the hospital; and Group III, cases under observation.

*Group I.*—There have been six deaths in cases not operated upon and four deaths following operations for bleeding ulcers. Of the six cases that died without operation, it is interesting to note that four of these had negative gastric histories. In spite of transfusions and other supportive measures, these cases resulted in fatalities and their conditions were such that operative intervention could not have been done. (See Table III.) There were also four post-operative deaths in cases operated upon for bleeding ulcers. In studying these cases it would seem that Case I, Table IV, should have been given a trial at medical treatment. Case III, Table V, with a definite ulcer at operation, which consisted of gastroenterostomy and appendectomy, died from pneumonia and no evidence of the ulcer was found at autopsy, this indicating that the ulcer had completely healed within five days. In view of

TABLE III

*Cases of Bleeding Ulcers Not Operated upon Resulting in Death*

| No. | Date              | Age | Sex | Past history   | Location of lesion | Previous treatment |
|-----|-------------------|-----|-----|--|--------------------|--------------------|
| 1   | July 8, 1911      | 60  | M   | Pain for nine months, vomiting blood, and blood in stools several days.  | Duodenum           | None               |
| 2   | December 14, 1925 | 43  | M   | Operated for perforated ulcer, November, 1922. Symptom-free until past six months. Now pain after meals. On admission to hospital vomited blood. | Duodenum           | Operation          |
| 3   | March 11, 1927    | 35  | M   | Pain in abdomen and vomiting for nine days but no blood.   | Duodenum           | None               |
| 4   | March 23, 1927    | 51  | F   | Vomiting blood twelve hours.   | Duodenum           | None               |
| 5   | August 8, 1927    | 44  | M   | Vomiting blood six hours.  | Gastric            | None               |
| 6   | August 20, 1929   | 56  | M   | Bleeding from rectum seven days.   | Gastric            | None               |



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TABLE III—*Continued*

| No. | Stay in hospital                 | Treatment in hospital   | X-rays   | Autopsy |
|-----|----------------------------------|---|----------|---------|
| 1   | 4 days. Died, July 12, 1911.     | Infusions and hypodermoclysis.  | None     | Yes     |
| 2   | 4 days. Died, December 18, 1925. | Infusions and one transfusion, 500 cubic centimeters.   | None     | Yes     |
| 3   | 4 days. Died, March 15, 1927.    | Profuse hæmorrhage, died within two hours.  | Negative | Yes     |
| 4   | 6 hours. Died, March 23, 1927.   | Infusion.   | None     | Yes     |
| 5   | 2 days. Died, August 10, 1927.   | Transfusion, August 8, 1927, 500 cubic centimeters.<br>Transfusion, August 9, 1927, 500                               | None     | Yes     |
| 6   | 3 days. Died, August 23, 1929.   | Infusions, transfusions, August 21, 1929, 500 cubic centimeters. Transfusion, August 23, 1929, 800 cubic centimeters. | None     | Yes     |

TABLE IV

## *Cases of Bleeding Ulcers Operated upon That Died*

| No. | Date             | Age | Sex | Past history   | Location of lesion | Previous treatment   |
|-----|------------------|-----|-----|--|--------------------|--|
| 1   | May 8, 1928      | 34  | M   | Seven years ago attacks began, with pain after meals for a few months. Another attack five years ago. Two weeks ago had a third attack, vomiting coffee-ground material and tarry stools. On leaving Cornell Clinic the day of admission, fainted and was brought to hospital. | Duodenum           | No regulated treatment, visited Cornell Clinic and X-rayed |
| 2   | February 6, 1929 | 48  | M   | Pain after eating with belching of gas for twenty-five years. Vomiting at intervals for two years. Tarry stools for seven days. Day of admission became dizzy, weak, and fainted.  | Duodenum           | No regulated treatment                                     |

| No. | Stay in hospital                             | Treatment in hospital  | X-rays                        | Autopsy |
|-----|--|--|-------------------------------|---------|
| 1   | 3 days. Died, May 11, 1928. Lobar pneumonia. | Operation, May 9, 1928, gastroenterostomy.   | Duodenal ulcer                | No      |
| 2   | 35 days. Died, March 11, 1929. Pneumonia.    | February 9, 1929. Transfusion, 500 cubic centimeters. Operation, March 8, 1929, partial gastrectomy. | Duodenal ulcer, March 5, 1929 | Yes     |

TABLE V

## *Cases of Bleeding Ulcers Operated upon That Died*

| No. | Date             | Age | Sex | Past history  | Location of lesion | Previous treatment     |
|-----|------------------|-----|-----|---|--------------------|------------------------|
| 3   | April 22, 1929   | 32  | M   | Pain after meals for one month. Tarry stools for several days.  | Duodenum           | No regulated treatment |
| 4   | February 3, 1930 | 59  | M   | Epigastric pain for one year. Positive X-rays for eight months before admission. Losing weight and vomiting blood for several days. | Gastric            | Advised as to diet     |

# BLEEDING GASTRIC AND DUODENAL ULCERS

TABLE V—*Continued*

| No. | Stay in hospital                                | Treatment in hospital  | X-rays   | Autopsy  |
|-----|---|--|--|--|
| 3   | 14 days. Died, May 6, 1929.<br>Lobar pneumonia. | Operation, May 1, 1929, gastroenterostomy, appendectomy. Found on anterior surface of first portion of duodenum an indurated area in which crater could be felt.   | April 28, 1929, duodenal ulcer                       | Yes. No evidence of duodenal or gastric ulcer. |
| 4   | 27 days. Shock.                                 | Operation, February 28, 1930. Partial gastrectomy. Transfusions, February 11, 1930, 500 cubic centimeters; February 13, 1930, 750 cubic centimeters; February 22, 1930, 600 cubic centimeters; February 28, 1930, 500 cubic centimeters. | June 26, 1929, ulcer of lesser curvature. Pars media | No   |

this fact, it might seem as if more conservative operations in Cases II and IV would not have been advisable.

*Group II.*—There were twenty-one cases in this group. Four cases which were operated upon for bleeding ulcers have not been followed. The type of operation can be seen in Table VI. There are four other cases that have

TABLE VI

*Cases Operated upon for Bleeding Ulcers But Not Followed*

| No | Date             | Age | Sex | Past history  | Location of lesion           | Previous treatment             |
|----|------------------|-----|-----|---|------------------------------|--------------------------------|
| 1  | May 15, 1911     | 47  | F   | Pain in abdomen and vomiting of food for thirteen years. Vomiting food on admission.                                    | Pyloric                      | No regulated medical treatment |
| 2  | October 6, 1911  | 21  | M   | Indigestion and abdominal pain for ten months. Vomiting of blood day of admission.                                      | Ulcer not found at operation | None                           |
| 3  | October 10, 1918 | 25  | F   | Gastric hæmorrhage three years before admission on two occasions. Pain for six months. Vomiting blood day of admission. | Gastric                      | None                           |
| 4  | May 1, 1924      | 35  | M   | Pain and discomfort for six months. Vomited blood just before admission.  | Gastric                      | None                           |

| No. | Stay in hospital                        | Treatment in hospital   | X-rays                                      | Follow-up    |
|-----|---|---|---|--------------|
| 1   | 18 days. Discharged, June 3, 1911.      | Operation, May 18, 1911. Gastroenterostomy.                           | None  | Not followed |
| 2   | 27 days. Discharged, November 3, 1911.  | Operation, October 9, 1911. Gastroenterostomy.                        | None  | Not followed |
| 3   | 60 days. Discharged, December 10, 1918. | Operation, November 14, 1918. Partial gastrectomy.                    | October 25, 1918, ulcer of lesser curvature | Not followed |
| 4   | 40 days. Discharged, June 9, 1924.      | Infusions for hæmorrhage. Operation, May 27, 1924. Gastroenterostomy. | May 20, 1924, ulcer of lesser curvature     | Not followed |

been operated upon for chronic ulcers without pre-operative histories of hæmorrhages but which have bled post-operatively. In Table VII, Case IV, it is interesting to note that for eighteen years following a gastroenterostomy for pyloric obstruction, the patient was symptom-free, after which time he

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TABLE VII

*Cases That Have Bled Since Being Operated upon for Chronic Ulcers*

| No. | Date              | Age | Sex | Past history  | Location of lesion   | Previous treatment  |
|-----|-------------------|-----|-----|---|----------------------|---|
| 1   | February 27, 1916 | 32  | M   | Stomach trouble four years. After operation symptom-free for six months. Pain for three months. Vomiting of blood for five weeks.   | Gastric              | Operated upon for acute perforated ulcer, May 29, 1915. Simple closure            |
| 2   | August 15, 1926   | 32  | M   | Pain for several years. After operation symptom-free until one month ago. Now has pain and vomiting blood for one month. Also blood in stools.  | Gastric and duodenal | Operation, April 1, 1926, gastroenterostomy. Followed. Sippy diet since operation |
| 3   | February 27, 1929 | 27  | M   | Stomach trouble ten years. Operated upon twice. Vomiting of blood few hours before admission.   | Duodenal             | Operated upon, November, 1924, exploratory. April, 1926, gastroenterostomy        |
| 4   | April 19, 1928    | 61  | M   | Operated upon, June 20, 1910, Carney hospital, Boston, for duodenal ulcer with pyloric obstruction. Well until two weeks ago. First noticed tarry stools followed in few days by abdominal pain which has continued. Stools continued tarry and this A. M. vomited blood. | Duodenal             | None since operation  |

| No. | Stay in hospital                               | Treatment in hospital   | X-rays  | Follow-up    |
|-----|--|---|---|--------------|
| 1   | 11 days. Discharged, March 10, 1916.           | Rest and Sippy diet. Operation advised. Refused.                                  | March 8, 1916, ulcer of lesser curvature.                         | Not followed |
| 2   | 3 days. Left, August 18, 1926, at own request. | Sippy diet and one infusion.  | March 15, 1926, gastric and duodenal ulcer                        | Not followed |
| 3   | 36 hours. February 28, 1929.                   | Vomiting blood four hours before leaving. Left at own request, February 28, 1929. | March 10, 1926, duodenal ulcer                                    | Not followed |
| 4   | 28 days. Discharged, May 17, 1928.             | Sippy diet.   | May 10, 1926, gastroenterostomy, stoma normal; duodenal deformity | Not followed |

TABLE VIII

*Cases Treated for Bleeding Ulcer But Not Followed*

| No. | Date              | Age | Sex | Past history  | Location of lesion | Previous treatment |
|-----|-------------------|-----|-----|---|--------------------|--------------------|
| 1   | February 25, 1911 | 30  | M   | Pain in upper abdomen for one year. Vomiting blood two days and vomiting.             | Duodenal           | None               |
| 2   | July 21, 1911     | 19  | M   | Pain for four weeks. Vomiting blood twenty-four hours.                                | Gastric            | None               |
| 3   | October 19, 1911  | 40  | F   | Discomfort for a few months. Vomiting of blood for twelve hours.                      | Gastric            | None               |
| 4   | January 19, 1912  | 19  | F   | Pain in epigastrium for two weeks. Bleeding from rectum and vomiting blood four days. | Gastric            | None               |

# BLEEDING GASTRIC AND DUODENAL ULCERS

TABLE VIII—*Continued*

| No. | Stay in hospital                                      | Treatment in hospital   | X-rays | Follow-up    |
|-----|---|---|--------|--------------|
| 1   | 32 days. Discharged, March 27, 1911.                  | Infusions and diet.   | None   | Not followed |
| 2   | 2 days. Discharged, July 23, 1911, at own request.    | Hypodermoclysis.  | None   | Not followed |
| 3   | 7 days. Discharged, October 26, 1911, at own request. | Diet and infusions.   | None   | Not followed |
| 4   | 60 days. Discharged, March 18, 1912.                  | Horse serum and infusions. Bled for seven days after admission. | None   | Not followed |

had a profuse hæmorrhage, whereas Case II began hæmorrhaging only three and one-half months following the operation. This leaves thirteen cases of bleeding ulcers that were treated by conservative measures but have not been

TABLE IX

*Cases Treated for Bleeding Ulcers But Not Followed*

| No. | Date               | Age | Sex | Past history  | Location of lesion | Previous treatment                |
|-----|--------------------|-----|-----|---|--------------------|-----------------------------------|
| 5   | September 28, 1913 | 31  | F   | Pain in upper abdomen three weeks. Vomited blood three weeks before admission and on admission.   | Gastric            | None                              |
| 6   | November 30, 1913  | 29  | F   | Pain in abdomen after meals for three months. Vomited blood one week before admission and tarry stools since.   | Duodenal           | None                              |
| 7   | February 13, 1914  | 27  | M   | Abdominal pain six days. Vomiting blood and tarry stools three days.  | Gastric            | None                              |
| 8   | September 7, 1915  | 32  | F   | Pain in upper abdomen for thirteen years. Vomited blood and in hospital thirteen years ago for same. No other bleeding until six hours before admission; vomited blood. | Duodenal           | For hæmorrhage thirteen years ago |

| No. | Stay in hospital                        | Treatment in hospital   | X-rays  | Follow-up    |
|-----|---|---|---|--------------|
| 5   | 14 days. Discharged, October 11, 1913.  | Fluids by mouth, ice cap to abdomen and infusions.  | October 9, 1913, gastric ulcer lesser curvature     | Not followed |
| 6   | 55 days. Discharged, January 23, 1914.  | Horse serum, December 3, 1913, 20 cubic centimeters; horse serum, December 4, 1913; transfusion, December 6, 1913, 900 cubic centimeters. | January 10, 1914, duodenal ulcer                    | Not followed |
| 7   | 17 days. Discharged, March 2, 1914.     | Horse serum, February 14, 1914, 20 cubic centimeters; infusions and diet.   | March 27, 1914, gastric deformity, lesser curvature | Not followed |
| 8   | 75 days. Discharged, November 18, 1915. | Horse serum three times; infusions and diet.  | September 16, 1915, duodenal deformity              | Not followed |

followed since leaving. See Tables VIII, IX and X. One case in this group is of interest. Case VIII, female, aged thirty-two years, had a gastric hæmorrhage thirteen years before admission and was treated in a hospital at the time but was symptom-free until six hours before admission.

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TABLE X

*Cases Treated for Bleeding Ulcers But Not Followed*

| No | Date              | Age | Sex | Past history   | Location of lesion | Previous treatment        |
|----|-------------------|-----|-----|--|--------------------|---------------------------|
| 9  | January 13, 1924  | 38  | M   | Pain in epigastrium for one year. Vomiting of blood twenty-four hours. | Duodenal           | None                      |
| 10 | February 13, 1927 | 28  | M   | Pain in abdomen and vomiting blood twenty-four hours.                  | Duodenal           | None                      |
| 11 | September 1, 1928 | 32  | M   | Negative.  | Duodenal           | None                      |
| 12 | August 12, 1929   | 38  | M   | Negative.  | Duodenal           | None                      |
| 13 | November 19, 1928 | 30  | M   | Pain in abdomen for eight months. Tarry stools for two weeks.          | Pyloric            | None, except examinations |

| No. | Stay in hospital                               | Treatment in hospital   | X-rays                             | Follow-up    |
|-----|--|---|------------------------------------|--------------|
| 9   | 8 days. Discharged, January 21, 1924.          | Transfusion, January 15, 1924, 900 cubic centimeters.                                 | January 20, 1924, duodenal ulcer   | Not followed |
| 10  | 1 day. Left at own request, February 14, 1927. | Sippy diet.   | None                               | Not followed |
| 11  | 20 days. Discharged, September 20, 1928.       | Hypodermoclysis, September 1, 1928, September 2, 1928, September 3, 1928; Sippy diet. | September 18, 1928, duodenal ulcer | Not followed |
| 12  | 3 days. Left at own request, August 15, 1929.  | Infusions and Sippy diet.   | None                               | Not followed |
| 13  | 7 days. Discharged, November 26, 1928.         | Infusions and Sippy diet.   | November 22, 1928, pyloric ulcer   | Not followed |

*Group III.*—There are now twenty-one cases of bleeding ulcers under observation in the Gastro-enterological Clinic of the Fourth Medical and Surgical Divisions. Of this number seven have been operated upon for bleeding ulcers. See Tables XI, XII and XIII. Case I has been operated upon twice for a bleeding ulcer: the first operation being a gastroenterostomy done in March, 1924, after which the patient continued to bleed, and a second operation, which was purely an exploration, performed August, 1927. The patient has been symptom-free for the past three years. By the greatest

TABLE XI

*Cases Operated upon for Bleeding Ulcers*

| No. | Date             | Age | Sex | Past history   | Location of lesion | Previous treatment                              |
|-----|------------------|-----|-----|--|--------------------|---|
| I   | January 23, 1924 | 57  | M   | (1) Bleeding from rectum ten days, also vomiting blood. Six years ago similar attack. Another four years ago. No pain or abdominal discomfort.<br>(2) Bleeding from rectum.<br>(3) Well until four days ago. Tarry stools and vomiting blood.<br>(4) Well since last discharge until today. Tarry stools and vomiting blood. | Duodenal           | Treated for hæmorrhage on two occasions at home |

# BLEEDING GASTRIC AND DUODENAL ULCERS

TABLE XI—*Continued*

| No. | Stay in hospital  | Treatment in hospital   | X-rays   | Follow-up   |
|-----|---|---|--|---|
| 1   | January 23, 1924 to February 21, 1924. Re-admitted, February 28, 1924. Discharged, March 24, 1924. Re-admitted, September 5, 1926, to September 24, 1926. Re-admitted, August 18, 1927, to October 7, 1927. | (1) January 25, 1924, transfusion, 600 cubic centimeters.<br>(2) Operation, March 6, 1924, gastroenterostomy.<br>(3) Transfusion, September 7, 1926, 400 cubic centimeters.<br>(4) Transfusion, August 20, 1927, 500 cubic centimeters.<br>(5) Operation, September 16, 1927, exploratory, found normal gastroenterostomy with duodenal ulcer but nothing done. | February 20, 1924, duodenal ulcer<br>September 31, 1926, stoma normal<br>January 4, 1929, gastroenterostomy. Stoma normal<br>May 15, 1930, gastroenterostomy. Stoma normal | No pain, vomiting or tarry stools since last operation. Last seen, September 11, 1930 |

stretch of the imagination the last operation could not have been a factor in the patient's condition during this period of time. Case VI also was of interest, as he had first a pyloroplasty for hæmorrhage and pain in December, 1925, then two years later, in January, 1928, a partial gastrectomy for pain, and again in December, 1929, he had several profuse hæmorrhages. There

TABLE XII

## *Cases Operated Upon for Bleeding Ulcers*

| No. | Date              | Age | Sex | Past history  | Location of lesion | Previous treatment   |
|-----|-------------------|-----|-----|---|--------------------|--|
| 2   | February 2, 1928  | 30  | M   | Six years ago pain and vomiting of blood and tarry stools. Medical treatment. Well two and one-half years, then another attack. Present attack one week ago, vomiting blood and tarry stools. | Duodenal           | Modified Sippy diet  |
| 3   | April 29, 1928    | 37  | M   | No history of abdominal pain. Vomiting blood and tarry stools three days before admission. Admitted in shock.   | Duodenal           | None   |
| 4   | September 6, 1928 | 30  | M   | (1) Patient has had pain for eight years after meals. Vomited blood day before admission.<br>(2) Since leaving hospital, pain after meals and tarry stools daily.                             | Duodenal           | In hospital eight years ago in California for three weeks. |

| No. | Stay in hospital  | Treatment in hospital  | X-rays   | Follow-up   |
|-----|---|--|--|---|
| 2   | February 2, 1928 to March 25, 1928.   | February 9, 1928, transfusion, 500 cubic centimeters. February 10, 1928, operation, cauterization of ulcer, gastroenterostomy and appendectomy.  | February, 7, 1928, duodenal ulcer<br>April 4, 1930, deformity first portion duodenum. Stoma normal | March 6, 1930, symptom-free since operation. Last seen, July 31, 1930   |
| 3   | April 29, 1928 to June 19, 1928.  | April 29, 1928, transfusion, 500 cubic centimeters. May 5, 1928, transfusion, 500 cubic centimeters. June 1, 1928, operation, cauterization of ulcer, gastroenterostomy and appendectomy.  | May 20, 1928, duodenal ulcer. July 15, 1930, duodenal deformity. Stoma normal                      | Symptom-free since operation. Last seen, October 2, 1930  |
| 4   | September 6, 1928 to September 24, 1928. Re-admitted, October 25, 1928 to November 9, 1928. | (1) On Sippy diet, developed severe pain. Diagnosis, perforated ulcer. Operation, September 9, 1928, exploratory, no ulcer found, nothing done.<br>(2) Operation, October 26, 1928, cauterizing of ulcer, gastroenterostomy and cholecystectomy. | September 25, 1928, duodenal ulcer   | After leaving hospital first time would not follow diet, used alcohol frequently. Returned, January 5, 1929, not following diet |

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TABLE XIII

*Cases Operated Upon for Bleeding Ulcer*

| No. | Date             | Age | Sex | Past history  | Location of lesion | Previous treatment  |
|-----|------------------|-----|-----|---|--------------------|---|
| 5   | August 27, 1927  | 42  | M   | Pains after eating for two years. Black stools at intervals. Vomiting blood before admission. | Duodenal           | None  |
| 6   | December 1, 1929 | 31  | M   | Pain in abdomen after meals for eleven to twelve years. Hæmorrhage, December 17, 1925.        | Duodenal           | December 17, 1925, transfusion, 700 cubic centimeters for hæmorrhage. Operation, December 28, 1925. Finney pyloroplasty. Re-operated upon January 8, 1928. Partial gastrectomy. Post-graduate Hospital. |
| 7   | January 29, 1930 | 45  | M   | Pains after meals for two years. Blood in stools and vomiting three hours before admission.   | Duodenal           | None  |

| No. | Stay in hospital                                | Treatment in hospital   | X-rays   | Follow-up   |
|-----|---|---|--|---|
| 5   | 31 days. August 27, 1927 to September 28, 1927. | Infusions and operation, September 1, 1927. Gastroenterostomy.  | February 7, 1930, ulcer first portion duodenum. Stoma normal | Symptom-free since operation. Last seen, August 2, 1930         |
| 6   | 24 days. Discharged, December 24, 1929.         | Transfused, December 4, 1929, 500 cubic centimeters; transfused, December 9, 1929, 500 cubic centimeters.   | August 15, 1930, partial gastrectomy. Stoma normal           | Symptom-free since leaving hospital. Last seen, October 2, 1930 |
| 7   | 36 days. Discharged, March 6, 1930.             | Transfused, January 29, 1930, 600 cubic centimeters; transfused, January 31, 1930, transfused, February 3, 1930, 350 cubic centimeters; transfused, February 10, 1930, 500 cubic centimeters; Operation February 14, 1930. Excision of ulcer and gastroenterostomy. | September 27, 1930, stoma normal. Duodenal deformity         | Symptom-free. Last seen, October 2, 1930                        |

are five cases that have bled while being treated for chronic ulcers under medical management in the clinic. Although they were progressing satisfactorily before the hæmorrhages they required hospital care while bleeding but have not been operated upon. Since their hæmorrhages they have re-

TABLE XIV

*Cases That Bled Under Medical Treatment in the Clinic*

| No. | Date           | Age | Sex | Past history   | Location of lesion   | Previous treatment   |
|-----|----------------|-----|-----|--|----------------------|--|
| 1   | April 28, 1928 | 26  | M   | Pain after meals for seven years. Tarry stools two weeks before entering hospital. | Duodenal             | Treated by physician before entering clinic, on milk diet. |
| 2   | March 16, 1929 | 56  | M   | Pain and discomfort in abdomen for ten years.                                      | Duodenal and gastric | No regulated treatment before entering clinic              |
| 3   | March 23, 1929 | 43  | M   | Pain after meals for one month.  | Duodenal             | No regulated treatment before entering clinic              |

# BLEEDING GASTRIC AND DUODENAL ULCERS

TABLE XIV—*Continued*

| No. | Stay in hospital                              | Treatment in hospital   | X-rays   | Follow-up  |
|-----|---|---|--|--|
| 1   | From October 6, 1929 to October 17, 1929.     | Sippy diet, ice cap to abdomen. Transfusion, 500 cubic centimeters.   | April 23, 1928, duodenal ulcer. October 26, 1928, same. October 23, 1929, same. March 15, 1930, same | No bleeding since leaving hospital but slight pain every few weeks. Last seen April 15, 1930   |
| 2   | From October 26, 1929 to November 17, 1929.   | Sippy diet. Transfusion, November 1, 1929, 500 cubic centimeters. Transfusion, November 6, 1929, 500 cubic centimeters. Operation advised, refused. | March 13, 1929, ulcer on lesser curvature and duodenal ulcer. October 15, 1929, same                 | Had a hæmorrhage, January 5, 1930 and taken to Fordham Hospital. Operation at Mt. Sinai Hospital, February 4, 1930, ca. of stomach. June 14, 1930, no complaints |
| 3   | From September 7, 1929 to September 28, 1929. | Sippy diet. Transfusion, September 9, 1929. Transfusion, September 15, 1929, 500 cubic centimeters.   | March 15, 1929, duodenal ulcer. September 8, 1930, duodenal ulcer                                    | October 7, 1930, no bleeding but some pain since leaving hospital, April 10, 1930  |

sumed satisfactory progress under medical care. (See Tables XIV and XV.) There are nine cases that were brought to the hospital for hæmorrhages that are now being followed in the clinic. These cases are, at the present time,

TABLE XV

*Cases That Bled Under Medical Treatment in the Clinic*

| No. | Date           | Age | Sex | Past history  | Location of lesion | Previous treatment  |
|-----|----------------|-----|-----|---|--------------------|---|
| 4   | May 25, 1929   | 41  | M   | No history of abdominal discomfort. History of tarry stools and vomiting blood. | Duodenal           | Transfused in January, 1928, also in March, 1929                    |
| 5   | April 28, 1928 | 26  | M   | Pain and indigestion for six years.   | Duodenal           | In clinic. Passed tarry stools, January 3, 1929 to January 20, 1929 |

| No. | Stay in hospital   | Treatment in hospital   | X-rays   | Follow-up                                |
|-----|--|---|--|--|
| 4   | January 17, 1928 to February 10, 1928. March 9, 1929 to March 29, 1929.                            | Sippy diet and transfusions.  | January 21, 1928, negative. March 21, 1929, duodenal ulcer. November 29, 1929, duodenal ulcer        | No bleeding since March 9, 1929          |
| 5   | April 25, 1929 to May 29, 1929. Profuse hæmorrhage ten days after operation for acute perforation. | Operation, April 25, 1929. Transfusion, May 5, 1929, 500 cubic centimeters. | April 8, 1928, duodenal ulcer. September 16, 1929, duodenal ulcer. April 3, 1930, duodenal deformity | Symptom-free. Last seen, August 28, 1930 |

symptom-free. (See Tables XVI, XVII and XVIII.) Careful laboratory work has been done on all the bleeding cases. Each case has had a gastric analysis, complete blood count, bleeding and clotting time, clot retraction time, platelet counts, complete blood chemistry including urea nitrogen, N. P. N., creatinine, chlorides, sugar, calcium and phosphorus, also urinalysis, Wasser-



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TABLE XVI

*Cases That Bled Without Previous Treatment*

| No. | Date              | Age | Sex | Past history   | Location of lesion        | Previous treatment   |
|-----|-------------------|-----|-----|--|---------------------------|--|
| 1   | April 14, 1928    | 60  | M   | Vomiting blood and tarry stools a few hours before admission.  | Duodenal                  | None   |
| 2   | December 30, 1928 | 32  | M   | (1) Pain after meals for two months.<br>(2) Gained forty pounds. No complaints until two months before admission. Vomiting blood seven days.   | Gastric. Lesser curvature | None   |
| 3   | February 24, 1929 | 46  | F   | Treated twenty-five years ago in Bellevue Hospital for an ulcer of stomach. In hospital few weeks. Symptom-free until two weeks ago; since then pain; vomiting blood two hours before admission. | Duodenal                  | Hospital treatment for ulcer twenty-five years ago. Well for twenty-five years |

| No. | Stay in hospital   | Treatment in hospital  | X-rays  | Follow-up   |
|-----|--|--|---|---|
| 1   | May 14, 1926 to May 26, 1926   | Sippy diet and infusions.  | May 25, 1926, duodenal ulcer. December 8, 1928, negative  | No vomiting of blood or tarry stools. Symptom-free, March 9, 1929   |
| 2   | December 30, 1928 to January 16, 1929. Re-admitted August 30, 1930 to September 13, 1930 | (1) January 7, 1929, transfusion, 450 cubic centimeters. Sippy diet.<br>(2) September 7, 1930, transfusion, 500 cubic centimeters. Sippy diet. | January 15, 1929, ulcer on lesser curvature of stomach. September 9, 1930, G. I. Negative. September 10, 1930, chest negative | Last seen, September 25, 1930                                       |
| 3   | February 24, 1929 to March 9, 1929   | Sippy diet; hypodermoclysis.   | March 8, 1929, duodenal ulcer. August 2, 1929, duodenal ulcer. July 22, 1930, negative  | No vomiting or tarry stools. Symptom-free. Last seen, July 31, 1930 |

mann and stool examination. All work was essentially negative except a low hæmoglobin and red blood count.

*Summary.*—Of the fifty-two cases reported in this paper, there were ten deaths, six of which were in cases treated by conservative measures, the deaths occurring in spite of supportive treatment. There were four post-operative

TABLE XVII

*Cases That Bled Without Previous Treatment*

| No. | Date              | Age | Sex | Past history  | Location of lesion | Previous treatment |
|-----|-------------------|-----|-----|---|--------------------|--------------------|
| 4   | March 31, 1929    | 29  | M   | (1) Pain in epigastrium for six or seven years.<br>(2) Vomiting blood two days.   | Pyloric            | None               |
| 5   | November 23, 1929 | 26  | M   | One year ago operated upon for chronic appendicitis. Going to work fainted on subway steps and cut his face. Vomited blood. | Duodenal           | None               |
| 6   | May 10, 1929      | 41  | F   | Pain after meals for three years which was relieved by soda. Vomiting blood and tarry stools for two days.                  | Duodenal           | None               |

# BLEEDING GASTRIC AND DUODENAL ULCERS

TABLE XVII—*Continued*

| No. | Stay in hospital  | Treatment in hospital  | X-rays  | Follow-up   |
|-----|---|--|---|---|
| 4   | March 31, 1929 to May 10, 1929. Re-admitted February 21, 1930 to March 11, 1930 | (1) Sippy diet and infusions.<br>(2) Sippy diet and infusions.     | April 15, 1929, pyloric ulcer. Refused others                                       | Patient began treatment May 11, 1929. Discontinued in a few weeks. Second hæmorrhage, February 21, 1930. Returns irregularly. |
| 5   | November 23, 1929 to December 16, 1929  | Transfusion, November 27, 1929, 500 cubic centimeters. Sippy diet. | November 30, 1929, ulcer, first portion of duodenum. August 5, 1930, duodenal ulcer | No complaints, except occasional pain. Last seen, October 2, 1930   |
| 6   | May 16, 1929 to May 24, 1929  | Infusions and Sippy diet.  | May 20, 1929, duodenal ulcer. March 11, 1930, duodenal ulcer                        | Gained fifteen pounds. No bleeding, only slight pain. Last seen, September 25, 1930   |

deaths, and it would seem that in two cases more conservative operations should have been done. In the twenty-one cases that have been operated upon or treated conservatively, but which have not been followed, there is little information that can be gained from the study of this group, except that the patients were discharged improved. Of the twenty-one cases now under observation in the clinic, it is interesting to note that five of these were being treated for chronic ulcers and progressing satisfactorily when they hæmorrhaged severe enough to confine them to the hospital while under our care.

TABLE XVIII

*Cases That Bled Without Previous Treatment*

| No. | Date             | Age | Sex | Past history   | Location of lesion | Previous treatment  |
|-----|------------------|-----|-----|--|--------------------|---------------------|
| 7   | January 4, 1930  | 22  | M   | Abdominal pain for six months. Tarry stools for two weeks.   | Duodenal           | None                |
| 8   | February 1, 1930 | 47  | M   | Fainted and fell at work; received lacerated scalp. Two dizzy spells few days before. Tarry stools after entering hospital.  | Duodenal           | None                |
| 9   | March 1, 1930    | 31  | F   | Pain in upper abdomen for twelve years. Vomiting of blood and tarry stools nine years ago. In bed ten days. Repeated about every three years since. Last two days ago. | Duodenal           | Modified Sippy diet |

| No. | Stay in hospital                             | Treatment in hospital   | X-rays   | Follow-up  |
|-----|--|---|--|--|
| 7   | January 4, 1930 to January 10, 1930 A. O. R. | Infusion and Sippy diet.  | January 20, 1930, duodenal ulcer                           | April 10, 1930. Social Service visit, moved                          |
| 8   | February 1, 1930 to February 20, 1930        | Transfusion, February 11, 1930, 500 cubic centimeters. Transfusion, February 15, 1930, 500 cubic centimeters. | March 8, 1930, duodenal deformity. July 15, 1930, negative | Improved, no complaints. Last seen, July 17, 1930. Gained ten pounds |
| 9   | March 1, 1930 to March 6, 1930 A. O. R.      | Hypodermoclysis and Sippy diet. Transfusion refused.  | April 10, 1930, duodenal ulcer                             | Improved, no complaints. Last seen, June 6, 1930                     |

Also, two cases have been operated upon for bleeding ulcers but have continued to bleed since their operations. During this period of nineteen and one-half years there have been ten full-attending surgeons responsible for the treatment of these cases and in view of that it would seem the treatment has been fairly uniform and the mortality of 19 per cent. not unduly high.

*Comment.*—After studying these cases, it may seem confusing to determine how bleeding ulcers should be treated, but, as has been noted, the cases of acute hæmorrhages that proved fatal in spite of conservative treatment usually occurred in patients with negative or short gastric histories. The cases with chronic recurring hæmorrhages can usually be controlled by conservative treatment but whether they are permanently cured cannot be stated at present. Surgery seems indicated in chronic hæmorrhages if the patient is incapacitated at frequent intervals. The type of operation can be decided upon only after exploring the lesion, but if possible the ulcer should be cauterized or excised, plus whatever operative procedure may seem indicated. It is very questionable whether partial gastrectomies are ever indicated in bleeding lesions, either of the stomach or duodenum.

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# SACRAL CHORDOMA

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FROM THE DEPARTMENT OF ORTHOPEDIC SURGERY OF THE CLEVELAND CLINIC

IN THE present paper, the writers offer another authentic case of chordoma to add to the rather meagre number now reported. A review of the literature has revealed accounts of only slightly more than eighty cases of all varieties. Most of these have been situated, as was this one, in the sacral area, the next most frequent site being the spheno-occipital region, although in the past few years some cases occurring along the spine at various levels have been reported. Probably, chordoma is not so rare as the number of reported cases indicates, many such tumors being either overlooked or incorrectly diagnosed.

*History of the Case.*—This patient was a man aged forty-one, a manufacturer, who came to the clinic September 10, 1929, complaining of pain in the lower part of his back. This pain began in December, 1928. It was very mild at first, but increased slowly in intensity. It was of a constant boring character not affected by activity, and interfered with the patient's sleep. Heat, aspirin, and periods of rest had failed to give relief and after months of annoying and unrelievable pain in the lower spine, occasionally radiating down the left leg, a consultation was sought.

The findings on physical, laboratory, and X-ray examinations were negative, except for a tender area the size of a fifty-cent piece over the lower third of the sacrum exactly in the mid-line. This area could be definitely delimited, and neither pressure over the surrounding parts nor manipulation of the lumbosacral or sacro-iliac joints produced any pain. Rectal examination revealed a bulging area on the anterior surface of the sacrum in its lower third which was tender and semifluctuant. There was no fixation of the soft tissues, and the coccyx was free and movable and not painful.

Exploration, September 14, 1929, revealed a tumor mass, yellowish, soft, and very friable, which protruded from the posterior surface of the sacrum and extended through to its anterior surface, the area of bone erosion being about 2 centimetres in diameter. A portion of the tissue was removed for pathological study, and frozen sections were made at this time but were not sufficiently clear to permit of a diagnosis. The tumor was curetted out as thoroughly as possible, its bed was packed with vaseline gauze, and the wound was closed.

Our pathologist, Dr. Allen Graham, reported that macroscopically, the specimen consisted of numerous grayish-pink pieces of tissue, soft, friable, and of a somewhat gelatinous consistency. Microscopically, the appearance of the tumor tissue was variable. There were areas in which small and large solid nests, strands, and masses of tumor cells were lying in a homogeneous pink-staining mucoid stroma. The tumor cells varied considerably in size and shape. In general, they were made up of a large amount of homogeneous, pink-staining cytoplasm, containing a relatively small, round, spindle-shaped, or irregular nucleus. The nuclei were vesicular, and had well-defined nucleoli. The cell outlines were not distinct. There were large masses of multinucleated cytoplasm which had the appearance of syncytial tissue. The cytoplasm was vacuolated in many instances. In some areas the tissue was made up of compact masses of spindle cells, forming fibrillæ and whorls, little of the mucoid stroma being present, and the picture was not unlike that seen in a fibroma or fibrosarcoma. The nuclei of the cells

were variable in size and shape, and a few mitotic figures and irregular nuclear divisions were observed. In other areas there was a mixture of the two histological types described above. In a few areas the arrangement of the tissue was somewhat suggestive of cartilage.

The pathological diagnosis was *sacral chordoma*.

September 19, 1929, the sacrum was radiated with 900 r-units. The patient was discharged from the hospital September 22, 1929. He was free from pain, but there was a slight seropurulent discharge from the wound. Subsequently he reported regularly for dressings and observation until March 10, 1930. Although there had not been any return of discomfort nor any external evidence of a recurrence of the tumor up to

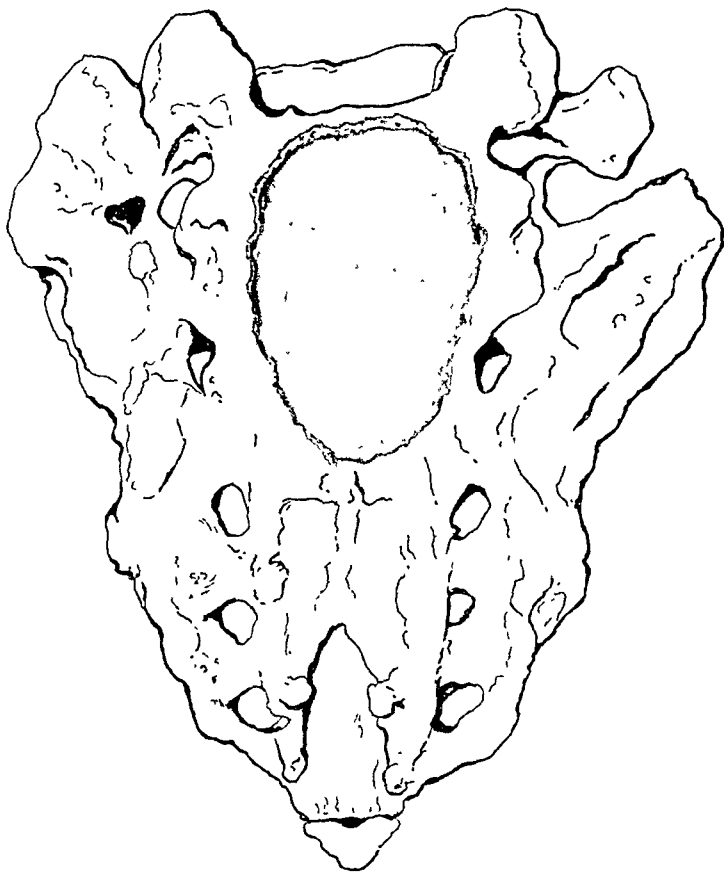


FIG. 1.—Drawing of sacrum showing the relative size and position of the chordoma at the time of the second operation.

this time, on rectal examination a mass was palpable which seemed to be slowly increasing in size. Another attempt at complete excision was therefore advised.

The second operation was performed March 27, 1930. Pre-operative rectal examination revealed a sessile mass in the hollow of the sacrum, about the size of a silver dollar and approximately 8 millimetres thick. The centre of this mass felt softer than the surrounding portion.

The old scar over the sacrum was excised. Considerable scar tissue was found under the skin. The spines of the sacrum were exposed with the periosteal elevator, and the ligamentous structures were reflected. There was a small opening into the sacral canal of about  $1\frac{1}{2}$  by 3 centimetres. Through this could be seen a soft mass, bluish-gray in color. The roof of the sacrum was cut away by rongeurs, leaving an opening

5 by 10 centimetres in size. The whole of the sacral canal was filled with a fairly firm, bluish-gray tumor mass, which was remarkably avascular except at the periphery (Fig. 1). In the lateral portion of the mass, bundles of tissue could be seen which were identified as the sacral nerves. The tumor apparently filled the entire sacral canal, and was intimately associated with the sacral nerves. It was deemed inadvisable, therefore, to attempt to remove it because of the probability that these nerves would be injured. A rectal examination was made at this juncture, and pressure was applied to the anterior aspect of the tumor in the hollow of the sacrum. This mass could be seen and felt to bulge slightly just to the left of the mid-line at about the mid-portion of the sacrum. The patient made a satisfactory operative recovery and was discharged from the hospital April 6, 1930.

Post-operative treatment consisted of deep X-ray therapy in doses of 160 r-units on April 26, May 3, May 10, May 24, and June 10, 1930. During this time the tumor progressively decreased in size, and gradually became harder and more calcified.

When last examined, September 9, 1930, the patient had continued free from pain, and rectal examination revealed that the tumor was definitely smaller, while all tenderness had disappeared. The X-ray treatments apparently had been successful in checking the development of the neoplasm. Metastasis is rare in this type of tumor, and none has been found in this case.

Chordoma is a tumor arising from cellular remains of the notochord, occurring, therefore, along the spine, most frequently at its extremities. It is composed of epithelial tissue, and is of endothelial origin.

As far back as 1856 Luschka described a case of chordoma, but did not recognize its origin or importance. Müller in 1858 suggested that the notochord was perhaps the origin of these tumors. The name "chordoma" was suggested by Ribbert in 1894. The development of our present knowledge has occurred almost entirely during the past thirty years, more particularly since 1922, when Professor Matthew J. Stewart, of Leeds, presented the first case recognized in Britain. In 1926 Professor Stewart collected fifty-seven reported cases, and in 1929 reports of only eighty cases had appeared in all the medical literature, and even some of these are questionable.

The average age at the onset of these tumors is from thirty-five to forty years, although cases have occurred as early as one and a half and as late as seventy-nine years. Spheno-occipital chordomas appear, on the average, ten years later than sacrococcygeal chordomas.

Males are twice as prone as females to develop these tumors, which suggests the part that trauma may play in their etiology. As a matter of fact, they have been produced experimentally in rabbits by puncturing the body of a vertebra.

The first symptom noticed usually is mild pain in the sacrum or lower portion of the spine, located exactly in the mid-line. Pain may radiate down the legs or into any region upon the nerve supply of which the growth encroaches. Relief cannot be obtained by the ordinary therapeutic measures, and the pain gradually increases until sleep becomes almost impossible. While the tumor may be discovered before the occurrence of pain, more often it is found as a result of the pain. The mass may protrude principally within the bony pelvis, and thus escape detection unless the sacrum is palpated

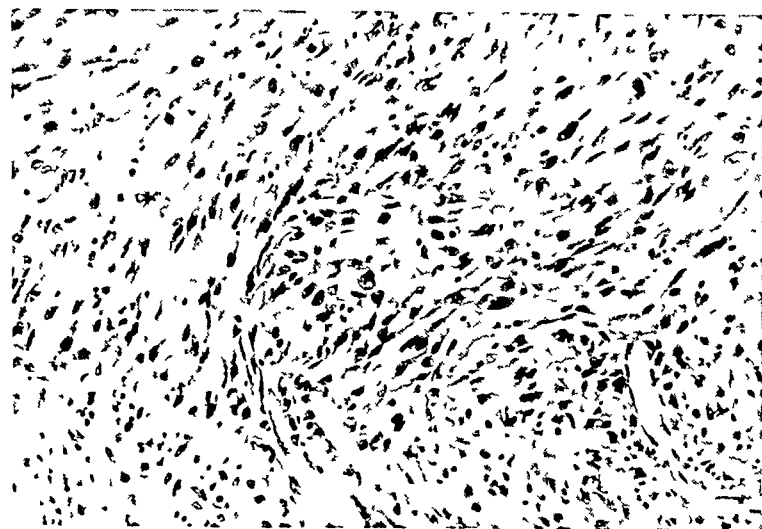


FIG. 2—View of a section, X 150, showing the spindle cell type of tissue

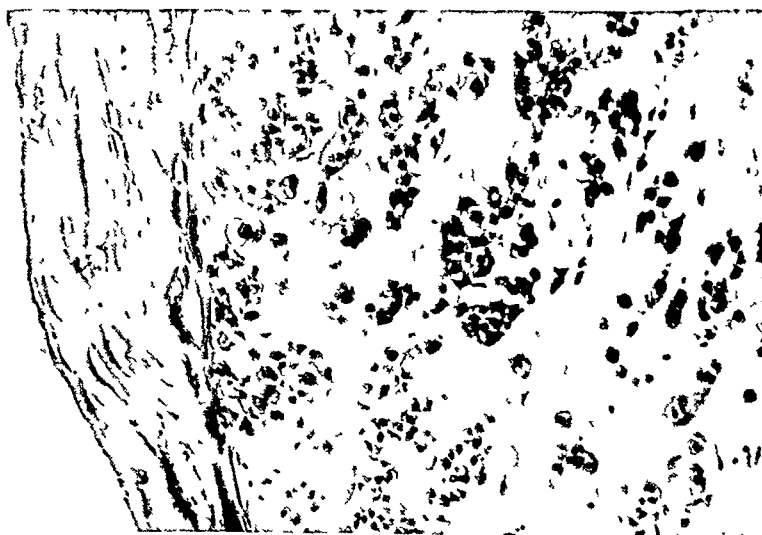


FIG. 3—View of a section, X 150, showing the fibrous capsule of the tumor and the cartilage like tissue with mucinous stroma.



FIG. 4—View of a section, X 600, showing the syncytial like masses of cells with vacuolated cytoplasm

by rectum. Chordomas grow very slowly, but their persistence has been regarded as certain.

Usually there are no symptoms except those caused by mechanical pressure. The diagnosis is suggested by the history of pain in the lower spine or skull and by the finding of a palpable tumor mass, semifluctuant in character. A positive diagnosis, however, can be made only by the microscopic appearance.

In 1926, Stewart and Morin described the gross appearance of these tumors in detail. The growth is well encapsulated, rounded, and lobulated. Gross section appears lobulated, and the lobules show mucoid degeneration, often of an advanced character. Frequently, cells of syncytial type are embedded in a sea of mucin. Some areas resemble colloid carcinoma, others cellular carcinoma. The salient microscopic features described by Stewart are as follows: alveolar character of growth; solid epithelial aspect of the younger cellular areas; cytoplasmic and intercellular vacuolation; formation intracellularly of mucinous fluid, which escapes from the cells to form, first, intercellular columns and, later, mucin in which only scattered cellular islets remain; rarity of mitotic figures except in very malignant cases. Chordomas are malignant only in a low degree, but occasionally they metastasize.

Although in the great majority of cases reported so far radiation has not helped, from the results in this case it is our opinion that the X-ray, in sufficient dosage, has greater possibilities than surgery. The end-result of our case, of course, is uncertain, but the improvement thus far has been satisfactory. The size of the tumor has decreased, the tissues have hardened, and all symptoms have disappeared.

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# THE SURGICAL TREATMENT OF SOME CONGENITAL ABNORMALITIES OF THE GENITO-URINARY TRACT\*

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THE most frequent congenital defects and abnormalities of the genito-urinary tract are hydronephrosis, undescended testicles (cryptorchidism), exstrophy of the bladder, hypospadias and epispadias. I think it can be accepted without debate that the surgical treatment of these abnormalities produces not only satisfactory, but, in many instances, surprisingly excellent, results.

In discussing the treatment of hydronephrosis, I intend to emphasize the benefits which can be obtained from conservative operations, such as (1) division of anomalous blood-vessels obstructing the passage of urine from the kidney into the ureter, (2) resection of hydronephrotic renal pelvis, preserving the kidney and establishing complete and efficient drainage of the kidney, and (3) division and reinsertion of the ureter into the dependent portion of a hydronephrotic renal pelvis.

In the treatment of exstrophy of the bladder and complete epispadias, with absence of urinary sphincters and lacking urinary control, transplantation of ureters into the rectum and the removal of the malformed bladder have changed the lives of the patients from one of embarrassment and seclusion to one of satisfactory progress. The rectum serves as a reservoir for collection of urine, efficiently controlled by a competent anal sphincter.

The undescended testicle (the condition of cryptorchidism) should be brought down and placed in the scrotum before the age of puberty, preferably between the ages of six and ten years, and by some method which will maintain the testicle in the depth of the scrotum, away from the spine of the pubic bone. Such a testicle placed in the normal position in the scrotum before puberty will increase normally in size, and should function satisfactorily, not only from the standpoint of the production of internal secretion from interstitial cells, but also from the standpoint of spermatogenesis.

Similarly, the surgical treatment of hypospadias and epispadias should be carried out at an early age, before puberty, and in our experience the best results are obtained in children between six and nine years of age. In the cases of hypospadias, the curved penis should be straightened, and then *later advancement of the urethra or the plastic development of an urethra* from the adjacent skin will, in many instances, give satisfactory results.

At this time, however, I wish to discuss in detail only cases of hydronephrosis, exstrophy of the bladder and cryptorchidism in which I have

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operated at The Mayo Clinic in the course of the last six years. The group includes twelve cases of exstrophy of the bladder, fourteen cases of hydronephrosis in which plastic operations have been successfully carried out, and thirty-six cases of undescended testicle. The patients in the first two groups have been carefully studied prior to and following operation so that the results obtained will be accepted, I believe, as evidence of what may be expected from such procedures.

*Hydronephrosis.*—Early work on plastic surgery of the hydronephrotic renal pelvis was done by Küster and by Fenger. The former advocated that a ureter which was laterally placed and was inefficiently draining the hydronephrotic pelvis be reimplanted in the dependent portion of the pelvis. He carried this out successfully in one case. Fenger suggested and carried out a plastic operation at the constricted ureteropelvic juncture, similar to the Heineke-Mikulicz pyloroplasty. The operation consisted of a longitudinal incision through the constricted portion which was sutured transversely. In 1917, impetus was given to plastic procedures on the renal pelvis by the report of a case by W. J. Mayo, in which, following most difficult pelviolithotomy, by accident, he completely detached the renal pelvis from the kidney. He reattached it to the kidney with interrupted sutures of catgut and covered the line of suture with a fatty fascial flap, and good union and function followed. Eight years before, W. J. Mayo, Braasch and MacCarty had reported a group of twenty-seven cases with hydronephrosis in which a plastic operation of the Heineke-Mikulicz type was successfully accomplished in nine cases. The following year this number had increased to sixteen.<sup>8</sup> In 1922, Quinby reported three cases of hydronephrosis, and in 1927, seven cases in which the ureter of the hydronephrotic renal pelvis was successfully transplanted to its dependent portion. At the Portland meeting of the American Medical Association in 1929, in collaboration with Braasch, I reported a group of four cases in which I had successfully resected hydronephrotic renal pelvises; Braasch had studied the pyelograms and the renal function before and after the operations. In that group was one patient who had bilateral hydronephrosis with infection. Prior to his operation, over a period of years, he had had a history of intermittent renal colic with chills, fever and lumbar pain. At first this had been controlled by drainage by ureteral catheter, but later this method became ineffective. The pelvis of the right kidney, with a capacity of 150 to 250 cubic centimetres of infected urine, and the left, of larger size, were resected two years ago, and the operations have been followed with excellent results. He has been reexamined within the last two months, and is in excellent condition, without further evidence of hydronephrosis or urinary retention in the kidneys.

When the hydronephrosis is bilateral, conservation of renal function becomes necessary. There have been five additional patients with bilateral hydronephrosis, one of whom has had the second renal pelvis successfully resected. The other four have had one renal pelvis resected and are waiting

a lapse of two or three months for the plastic operation on the other kidney.<sup>15</sup> In an additional case, in a woman with bilateral hydronephrosis, there was huge dilatation of the pelvis and calices of the left kidney. An attempt was made to reduce the size of the kidney by first establishing adequate drainage from the kidney into the ureter, and secondly, by the introduction of a tube through the cortex into the renal pelvis by nephrostomy. Angulation of the ureter by peripelvic connective tissue was the cause of the obstruction at the ureteropelvic juncture; this was successfully overcome by division of this peripelvic tissue. The pelvis and calices of this kidney have decreased in size more than 75 per cent. since these surgical procedures, as shown by pyelograms. It may be possible in selected cases to carry out similar procedures satisfactorily rather than to resect the pelvis.

*Exstrophy of the Bladder.*—Although exstrophy of the bladder is not common, 100 patients with this congenital abnormality have been operated on at the clinic in the last thirty years. Seventy-three of these patients have been operated on by a method described in 1917 by C. H. Mayo. The method consists of transperitoneal transplantation of the ureters into the sigmoid, using a principle which Coffey<sup>2</sup> described in transplantation of the common bile duct. The lower end of the uretèr, for a distance of 2.5 to 3 centimetres, is carried in the wall of the sigmoid, between the muscular and mucosal layers of the intestine, so as to secure a valve-like action. This method, in our experience at the clinic, has been attended by an extremely low mortality rate, and the evidences of ascending infection into the kidneys are almost wholly lacking, even after a period of as long as fifteen or twenty years following the operation. In two instances, following successful procedures of this type, the patients, who were women, were married and gave birth to children. One of these patients, a graduate nurse, gave birth to twins by Cæsarean section; the other was delivered of a normal baby at full term. Many of the patients operated on have been adults, but the best time to carry out the operative procedure is before the age of puberty. It is important, however, that the patients be at least four years of age and that they shall have obtained sphincteric control of the fæces. Although of late, bilateral simultaneous transplantation of the ureters into the sigmoid has been suggested and carried out in some cases,<sup>3</sup> in our experience, the safest procedure in children has been to transplant one ureter at a time. Preferably, the right ureter is transplanted at the first operation, and ten days or two weeks later, the left; ten days following, the bladder can be removed. Of the seventy-three patients on whom both ureters have been transplanted, three died in hospital, a mortality of 4.1 per cent. Sixteen other patients have been operated on by various methods: six by the method of bilateral simultaneous transplantation of Coffey, two by the method of Moynihan, and in eight cases a unilateral transplantation was done. These cases are not included in the series of seventy-three. In the series of twelve cases of exstrophy of the bladder which I am reporting, there have been no deaths.

*Undescended Testicles (Cryptorchidism).*—The preferable age for operation on these patients is between six and nine years. The testicle may lie within the abdomen, in the inguinal canal, or at the external inguinal ring. All cases of intra-abdominal testicle are associated with hernia, and in many instances in which the testicles are in the inguinal canal, a hernial sac is present. This hernial sac must be excised and the inguinal canal must be partially closed as a part of the plastic operation for cryptorchidism. One of the prerequisites for a satisfactory operation for cryptorchidism is that after the division of connective tissue around the vas deferens and the spermatic artery, the structures of the spermatic cord be of sufficient length to enable one to place the testicle in some part of the scrotum. In addition, it must be so placed in the scrotum that it is not in contact with the spine of the pubic bone, where it is more susceptible to injury than if it were intra-abdominal or in the inguinal canal. In any operative procedure intended adequately to correct the position of undescended testicles, the scrotum should be stretched to sufficient size to allow the testicles to be placed in its dependent portion, which keeps the testicles away from the spine of the pubic bone. In our experience, two operative procedures satisfy these requirements. In one, which is used by Cabot, traction is placed on the testicle and part of the scrotum by an elastic rubber band which is tied to a suture that extends through the gubernaculum and lower part of the scrotum; the rubber band is temporarily fastened to a metal crutch that bears on the perinæum in such a way that traction can be maintained. A second method which we have found to be very successful is similar to a method described by Keetley, and by Torek, and popularized by Meyer. It consists of an operation in two stages. At the first stage the testicle is brought out through an incision in the scrotum and is attached to the fascia lata of the thigh. Following this procedure, the patient is able to return to work or other activities within a period of two weeks. Two or three months later, or at any convenient time thereafter, the second stage of the operation is carried out, in which the scrotum is separated from the skin of the thigh and the testicle from the fascia lata of the thigh. It will then be found that the testicle can be replaced in the depth of the dilated portion of the scrotum when the incision of the scrotum or thigh is closed. The patient is usually able to leave the hospital the day following the second stage of the operation, which can be carried out satisfactorily under local anæsthesia.

## SUMMARY

In pre-operative and post-operative studies of patients on whom plastic operations for hydronephrosis have been accomplished, indications are that a conservative operation for hydronephrosis can be carried out successfully if sufficient renal parenchyma remains. These plastic operations, in my experience, have consisted for the most part of resection of the hydro-nephrotic portion of the renal pelvis and changing the angle of insertion of the ureter so that it completely and satisfactorily drains the dependent por-

tion of the renal pelvis. If the hydronephrosis is bilateral, such conservative procedures are operations of necessity. In a group of fourteen cases in which the renal pelvis has been resected, hydronephrosis was bilateral in five.

In the treatment of exstrophy of the bladder, transplantation of the ureters into the sigmoid, with subsequent removal of the bladder, is followed by excellent results. The rectum serves as a reservoir for the urine and almost without exception the patients on whom the procedure is carried out are able to hold the urine in the rectum without leakage for from four to six hours during the day. Many of them are able to retain the urine in the rectum the entire night. Experience has led us to the belief that the safest method of ureteral transplantation is one described by C. H. Mayo, in 1917, in which the ureters are transplanted separately with an interval of ten days or two weeks between each transplantation. Carrying the ureter between the mucosal and muscular layers of the sigmoid or rectal wall, which is Coffey's principle in transplantation of the common bile duct, has, by valve-like action, prevented ascending infection to the kidneys in practically all of the cases. Clinical evidences of this may be found in the general feeling of "good health" with normal growth in children, and the absence of lumbar pain, chills, or fever. In many cases fifteen to twenty years have elapsed since the ureterosigmoidal transplantation.

In the treatment of undescended testicle the testicle must be placed in the dependent portion of a scrotum of normal size, so that the testicle will not be in contact with the spine of the pubic bone. This has been successfully accomplished by the methods described by Cabot and by Torek. In Cabot's method the scrotum is stretched and the spermatic cord is lengthened by a one-stage operation in which an elastic band is temporarily used as a tractor. Torek's operation is in two stages. In the first stage the testicle is temporarily attached to the fascia lata of the thigh, and the skin of the thigh and the scrotum is attached around the testicle. After the second stage of the operation, when the scrotum is severed from the skin of the thigh and the testicle from the fascia lata of the thigh, the testicle will lie in the dependent portion of a scrotum of normal size. This procedure has been carried out in thirty-six cases with excellent results.

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## SOLITARY CYSTS OF THE KIDNEY

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FROM THE CLEVELAND CLINIC

BECAUSE of the apparent rarity of solitary cysts of the kidney it seems worth while to report ten cases from the records of the Cleveland Clinic. I use the term "apparent rarity" because it would appear that solitary cysts of the kidney are of more frequent occurrence than we are led to believe from a review of the literature. As Branch<sup>1</sup> states, solitary cysts of the kidney are rarely observed by the clinician but are frequently observed by the pathologist. He states further that unless the cysts reach a sufficient size to produce pressure symptoms, they are rarely diagnosed and are found only at autopsy. Branch states that they are present in from 3 to 5 per cent. of all

autopsies. In five kidneys from thirty-six cadavers, Kampmeier<sup>2</sup> found cysts which varied from 2.5 to 5 centimetres in diameter. From 2,610 autopsies at the Middlesex Hospital in London Morris<sup>3</sup> reported five cases of solitary cysts. We have found in the literature reports of 158 cases. The addition of our ten cases brings the total number to 168.

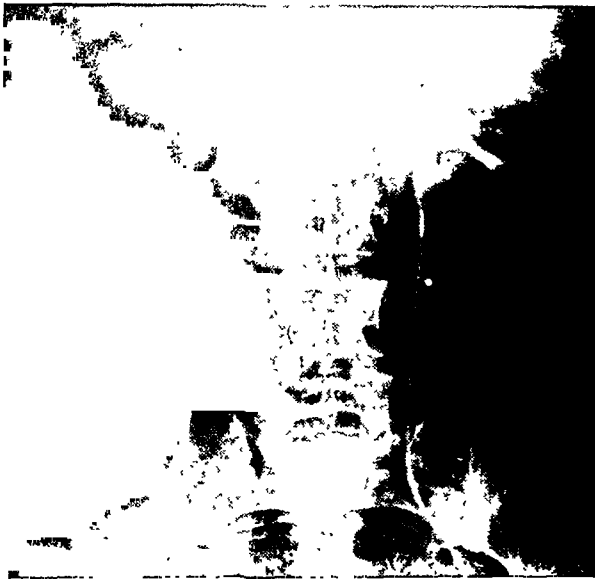


FIG. 1.—Pyelogram showing deformity of calyces of kidney due to solitary cyst.

years she had suffered from pain in the right side and difficulty in urination, the latter symptom having followed childbirth. The patient also had a feeling of fulness in the abdomen and an occasional aching pain in the right side. For the preceding few years there had been marked urgency and nocturia. There was no history of hæmaturia.

The physical findings were normal except for a palpable smooth mass in the region of the right kidney. The röntgenogram showed a large round shadow connected to the lower pole of the right kidney. The first pyelogram was normal, but a later one showed a spherical enlargement below the lower pole of the kidney (Fig. 1). Blood-pressure was 120/75, red blood count 4,400,000, white blood count 8,750, hæmoglobin 80 per cent., urine normal, Wassermann negative. The pre-operative diagnosis was cyst of the right kidney. At operation a cyst was found at the lower pole of the right kidney. This was removed together with a wedge of renal parenchyma. Convalescence was uneventful.

CASE I.—The patient was a woman forty years of age who entered the clinic complaining that during the preceding ten

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CASE II.—A man, sixty-two years of age, entered the clinic complaining of jaundice which had been increasing in intensity during the preceding few weeks, but was not associated with pain. There was marked pruritus and the stools were clay-colored. For years he had been aware of a mass in the right side of the abdomen which had been diagnosed "ptosed liver." It had not caused pain but only a feeling of fulness.

Physical examination revealed a man in very poor physical condition who was quite jaundiced and acutely ill. In the right kidney region was a large round mass the size of a grapefruit, which was not nodular and was soft in consistency. Pyelography was not thought advisable. The blood-pressure was 140/90. Laboratory findings were as follows: hæmoglobin 80 per cent., red blood count 4,030,000, white blood count, 6,950; blood urea 84; blood cholesterol 182; serum bilirubin 3.8 direct; urine—albumin two plus, 2 to 5 pus cells per high-power field, few granular casts; Wassermann negative.

A diagnosis of carcinoma of the head of the pancreas was made and an exploratory operation performed. In addition to carcinoma of the pancreas a large solitary cyst the size of a grapefruit was found at the lower pole of the right kidney. This was aspirated. The patient died a few days later of uræmia.

CASE III.—A man aged seventy-four entered the clinic complaining of nocturia, frequency, difficulty in voiding, and blood in the urine. Recently he had noted terminal hæmaturia. He was poorly nourished; blood-pressure was 130/80. The only important finding on general and cystoscopic examination was marked enlargement of the prostate. *Laboratory findings.*—Hæmoglobin 85 per cent., red blood count 4,350,000, white blood count 5,800; phenolsulphonphthalein 40 per cent. in two hours; blood urea 57; urine—albumin two plus, red blood cells 20 to 30, and white blood cells 2 to 5 per high-power field; Wassermann negative.

A suprapubic prostatectomy was performed, and the patient died four days later of pneumonia. Post-mortem examination revealed a cyst of the lower pole of the right kidney which was filled with light amber-colored serous fluid. Pneumonia was the primary cause of death.

CASE IV.—A man, seventy-nine years of age, entered the clinic complaining of difficulty in voiding. Five years ago he had first experienced increasing nocturia and difficulty in starting the stream which had diminished in size; terminal dribbling was quite pronounced. A poorly nourished man showing evidence of considerable loss in weight. Blood-pressure was 120/80. Heart moderately enlarged and a loud systolic blow was heard at the apex. Rectal examination revealed considerable enlargement of the prostate and cystoscopic examination showed marked intravesical projection of the prostate.

A perineal prostatectomy was performed. The patient died five days later of uræmia and pneumonia.

At post-mortem examination a large solitary cyst 18 centimetres in diameter and filled with serous fluid was found on the anterior surface of the upper pole of the right kidney.

CASE V.—A man, twenty-four years of age, entered the clinic complaining of pain in the left kidney region which had continued intermittently for the preceding year. These attacks came on suddenly, lasting from ten to fifteen minutes and then subsiding. There was no hæmaturia or passing of gravel. Nothing of significance was found in the physical examination; no tumor mass was palpable. The cystoscopic examination led to the diagnosis of calculous pyonephrosis. *Laboratory findings.*—Wassermann negative; blood normal; function test not recorded; urine—numerous pus cells, no red blood cells. A left nephrectomy was performed and in addition to the calculous pyonephrosis a cyst the size of a lemon was found at the lower pole of the kidney. Convalescence was uneventful.

CASE VI.—A man, forty-six years of age, entered the clinic complaining of severe attacks of pain over the right kidney from which he had suffered for several years. The pain radiated downward toward the scrotum. There was no history of hæmaturia or



passing of gravel. Physical findings were normal except for tenderness on deep pressure over the right kidney. *Laboratory findings.*—Wassermann negative, phenolsulphonphthalein 50 per cent. in two hours. Urine—trace of albumin, white blood cells 2-4 per high-power field. A cystoscopic examination was done and a diagnosis of calculous pyonephrosis was made from the pyelogram.

A right nephrectomy was performed at which time a large solitary cyst containing clear, serous fluid, was found at the lower pole of the kidney in addition to the calculous pyonephrosis. This cyst was ruptured accidentally while removing the kidney.

CASE VII.—A woman, forty-five years of age, entered the clinic complaining that for six months she had experienced urinary urgency, frequency every fifteen minutes and nocturia ten to twelve times. One month before entering the clinic she had passed a small amount of blood. There was no history of loss in weight. Two weeks previously she had had an attack of pain in the right side accompanied by chills and fever. She was a fairly well-nourished woman showing no evidence of weight loss. The blood-pressure



FIG. 2.—Photograph showing a large cyst of the right kidney associated with tuberculosis.



FIG. 3.—Photograph of cut specimen of kidney with cyst attached.

was 130/90. Suprapubic tenderness was present. Vaginal examination revealed a hard, pencil-like, tender lower right ureter. A cystoscopic examination was made and tubercle bacilli were found in the specimen from the right kidney. From the pyelogram a pre-operative diagnosis of tuberculosis of the right kidney was made. *Laboratory findings were as follows.*—Wassermann negative; hæmoglobin 70 per cent., red blood count 4,420,000, white blood count 7,800; urine—pus two plus, red blood cells 5-10 per high-power field, phenolsulphonphthalein 18 per cent. in fifteen minutes.

Nephrectomy was performed. The kidney was found to be tuberculous and a solitary cyst larger than an egg and containing yellowish, clear, serous fluid was found in the lower pole. Convalescence was uneventful. (Figs. 2 and 3.)

CASE VIII.—A man, sixty-four years of age, entered the clinic complaining of weakness and loss of weight. His general condition had been very poor for the preceding month and he had lost 20 pounds in weight.

He was very poorly nourished with a generalized glandular adenopathy. Blood-pressure was 124/80. The liver and spleen were both palpable.

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*Laboratory findings were as follows.*—Hæmoglobin 70 per cent., red blood count 3,900,000, white blood count 70,000, smear of blood showed 71 per cent. large lymphocytes; urine—albumin one plus, white blood cells two plus; Wassermann negative. A diagnosis of lymphatic leukæmia was made and X-ray therapy was instituted. The patient died two months later. At post-mortem a large solitary cyst filled with clear, serous fluid was found at the upper pole of the left kidney (Fig. 4).

It is interesting to note that a single cyst 3 centimetres in diameter containing clear, serous fluid was also found in the left lobe of the liver (Fig. 5). No other cysts were found.

CASE IX.—A man, fifty-three years of age, entered the clinic complaining of stomach trouble, the symptoms of which had been present during the preceding two years. During this time he had had more or less constant pain in the left lower quadrant which he described as a pulling-down pain. About one year ago he had had an attack of cramp-like pains in the left lower quadrant causing him to double up in agony, and six months previously he had had an acute attack of pain in the lower abdomen accompanied by vomiting.

He was well-nourished. Blood-pressure was 134/80. On physical examination

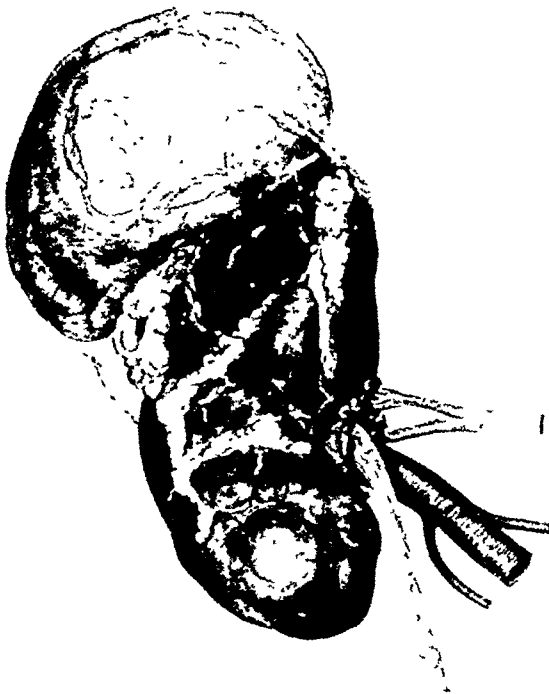


FIG. 4.—Photograph of cyst attached to upper pole of left kidney found post-mortem in a patient who died of lymphatic leukæmia.



FIG. 5.—Photograph of section of liver in which a cyst was found coincidentally with kidney cyst. (See Fig. 4.)

the only finding of significance was a mass to the left of the umbilicus. This mass was round, movable, and not tender. A pyelogram showed a large mass connected with the lower pole of the left kidney. *Laboratory findings.*—Red blood count 4,780,000, white blood count, 7,800, hæmoglobin 85 per cent; urine normal except for a few pus cells; blood urea 48; phenolsulphonphthalein test showed normal excretion.

A pre-operative diagnosis of solitary cyst of the lower pole of the left kidney was made. At operation a cyst the size of a small grapefruit was found attached to the lower pole of the left kidney (Figs. 6 and 7). This was excised without removing any of the kidney parenchyma. Convalescence was uneventful.

CASE X.—A boy, three years of age, was brought to the clinic because of an enlargement of the abdomen. He had always been healthy but the abdomen had been protuberant since birth (Fig 8).

On physical examination the only significant finding was a large mass the size of a grapefruit in the left hypochondrium. Upon röntgenographic examination this was shown to be a large mass in the region of the left kidney. Kidney function was normal as were the urinary findings. A pycelographic examination was not made.

A pre-operative diagnosis of malignant tumor of the kidney was made. At operation a large cyst 13 by 10 by 9 centimetres filled with serous fluid was found at the lower pole of the left kidney and extending upward on its lateral surface. As the kidney appeared to be atrophic it was removed with the cyst. The kidney and cyst together weighed 570 grams. Convalescence was uneventful.

*Review of the Literature.*—Solitary cysts of the kidney were first described by Fabry<sup>4</sup> in 1624. Thomas Willis,<sup>5</sup> the English clinician, described them in the seventeenth century, and in 1837 Rayer<sup>6</sup> first classified the various types, this classification being followed in 1876 by an excellent treatise by Lavan<sup>7</sup> in which he discussed the difference between solitary cysts of the kidney and polycystic kidney. In a complete review of the literature in 1906, Simon<sup>8</sup> collected fifty-two cases which had been reported from 1860 up to that time. Later, individual cases were cited and the literature was reviewed by Caulk,<sup>9</sup> Cunningham,<sup>10</sup> Blanchard,<sup>11</sup> Vogel,<sup>12</sup> Beneke,<sup>13</sup> Wulff,<sup>14</sup> Fowler,<sup>15</sup> and others.

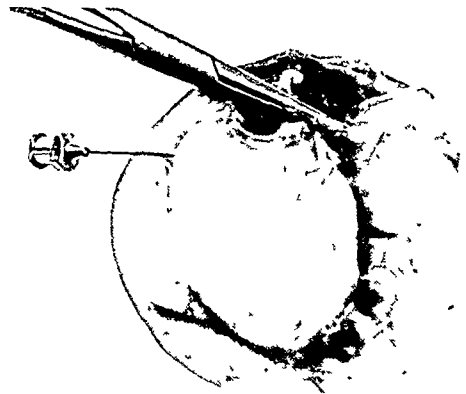


FIG. 6—Photograph of serous cyst of left kidney. FIG. 7—Photograph of this cyst after it was removed

In 1920 Kretschmer<sup>16</sup> again reviewed the literature adding forty-eight cases, including one of his own, to Simon's series, making a total of 100 cases.

McKim and Smith<sup>17</sup> in 1924 collected 117 cases from the literature, and added three. In the same year Harpster<sup>18</sup> presented ninety-five collected cases, in eighty-two of which an operation had been performed with the following results:

In thirty cases nephrectomy was done followed by recovery in twenty-three cases; in thirty-four cases, resection of the cyst alone, or together with a portion of the kidney, resulted in death in three cases or 9 per cent.; in four cases the cyst was tapped followed by death in two cases. In the remaining fourteen cases the type of operation was not stated.

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In 1928, Carson<sup>19</sup> collected 126 cases from the literature and added fifteen cases which had been reported between the years 1923 and 1927. These, with four additional cases made a total of 145.

In 1930, Grove<sup>20</sup> collected 153 cases from the literature, and added a case, and Kretschmer<sup>21</sup> recently reported five cases of his own. As we have

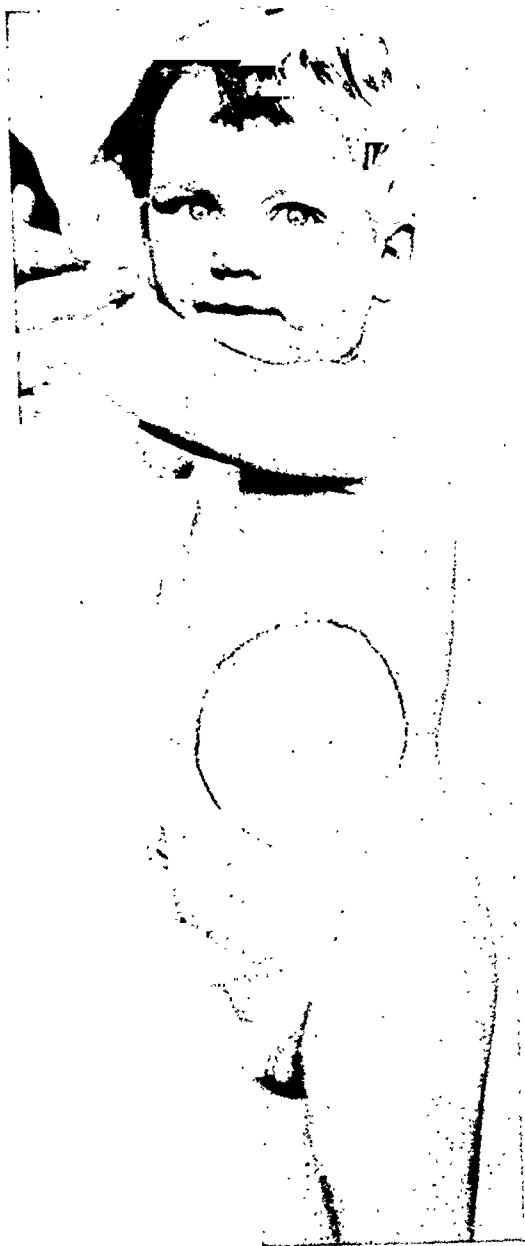


FIG. 8.—Photograph of a boy three years old in whose case a diagnosis of malignant tumor of the kidney was made. Operation disclosed a cyst 13 by 10 by 9 centimetres.

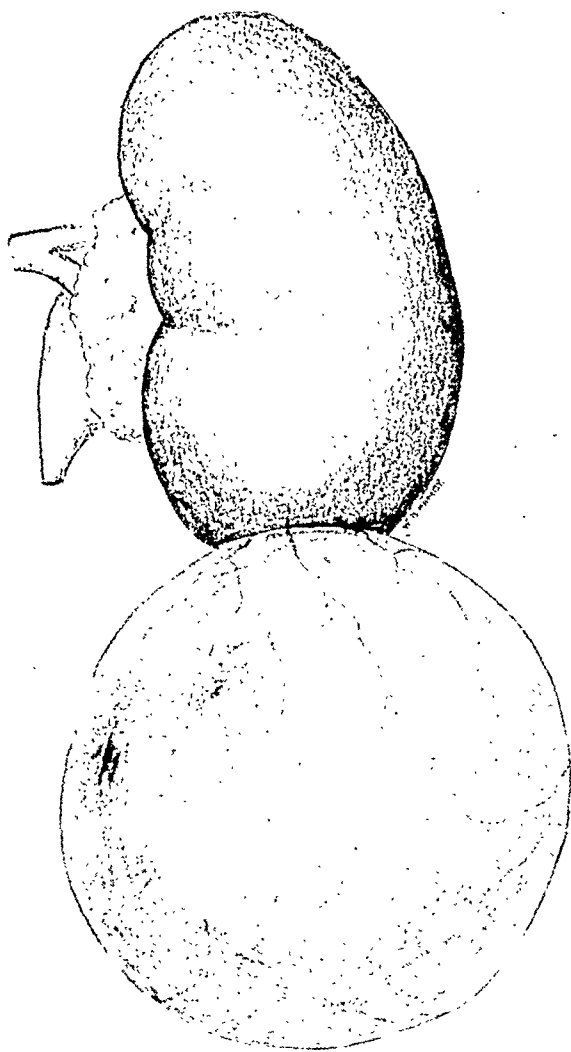


FIG. 9.—Drawing showing a solitary cyst at lower pole of kidney.

stated the addition of the ten cases cited in this paper brings the total number up to 168.

*Structure.*—The wall of a solitary cyst of the kidney is generally grayish-white in color varying from one to five millimetres in thickness. Calcification is rare but may occur as in the case cited by Kirwin.<sup>22</sup> The inner surface is smooth and glistening and fine blood-vessels may be seen coursing through it

(Fig. 9). The wall of the cyst is independent of the capsule of the kidney, although frequently it is closely adherent to it. Some investigators state that the cyst has no epithelial lining while others describe the presence of a single layer of low, cuboidal epithelium. It has even been stated that the lining consists of normal cell formation of uriniferous tubules which, as the result of pressure, may be flattened.

In our series of cases the cell lining of the cysts varied. In one case the lining consisted of flattened cells separated by rather heavy connective-tissue trabeculæ. In another, the cyst wall was composed of fairly dense, fairly well vascularized, simple, fibrous, connective tissue but no epithelial cells were present. If the cyst is large, pressure atrophy may be present in the adjacent kidney tissue.

A cyst usually contains clear, straw-colored, serous fluid the specific gravity of which is low. Hæmorrhage may take place into the cyst, producing blood clots. In one of our cases the fluid had a distinct odor of urine. Fowler states that the fluid contained in a cyst is clear, watery and albuminous, and does not contain urinary elements unless it communicates with the pelvis or calyces of the kidney, which is not the case as a general rule.

*Age Incidence.*—Carson states that the majority of cases of solitary cysts of the kidney occur between the ages of thirty and sixty years, the average age being forty-five. Simon also states that the condition occurs most frequently in the fourth and fifth decades. In Kretschmer's review of forty-two collected cases in which the age was stated, thirty-six cases occurred after thirty years of age. The youngest patient was sixteen months old (reported by Albarran and Imbert). In our series, the youngest patient was three years of age and the oldest seventy-nine. The age incidence in our series was as follows:

| <i>Age</i>            | <i>Number of Cases</i> |
|-----------------------|------------------------|
| 3 years . . . . .     | 1                      |
| 24 years . . . . .    | 1                      |
| 40-50 years . . . . . | 3                      |
| 51-60 years . . . . . | 1                      |
| 61-70 years . . . . . | 2                      |
| 71-80 years . . . . . | 2                      |

*Sex Incidence.*—Of the cases reviewed by O'Neil<sup>23</sup> in the Massachusetts General Hospital, five occurred in men and four in women. Of those reported by Albarran and Imbert<sup>24</sup> thirteen occurred in men and ten in women. In Kretschmer's series of cases twenty occurred in men and twenty-two in women, and in our series eight occurred in men and two in women. In Simon's<sup>8</sup> series, the condition occurred twice as frequently in women as in men. It is also interesting to note that most of the women in which the condition has been present were multiparous. In Carson's<sup>19</sup> series of 146 collected cases, eighty-nine occurred in women, forty-one in men and in sixteen cases the sex was not stated.

## SOLITARY CYSTS OF THE KIDNEY

*Location and Size.*—In six of the cases herein reported the cyst occurred on the right kidney and in four it was found on the left, while in Kretschmer's collected series, in twenty-one cases the cyst occurred on the right and in twenty on the left kidney. Carson has found that the condition occurs more frequently on the right kidney. Solitary cysts of the kidney are usually unilateral although Cunningham and Zaccarini<sup>25</sup> reported the occurrence of bilateral cysts. It is well known that small cysts are frequently found on arteriosclerotic kidneys but these are not solitary cysts and should not thus be included in this discussion. In the cases reviewed by McKim and Smith the site of the cyst was as follows:

|                       | <i>Lower pole<br/>of kidney</i> | <i>Upper pole<br/>of kidney</i> | <i>Center of<br/>kidney</i> |
|-----------------------|---------------------------------|---------------------------------|-----------------------------|
| McKim and Smith ..... | 51                              | 21                              | 8                           |
| Kretschmer .....      | 13                              | 11                              |                             |
| Higgins .....         | 7                               | 3                               |                             |

Solitary cysts may arise from the upper or lower pole, the anterior surface or the hilus of the kidney. In most of the cases reviewed herein the cyst was present on the lower pole of the kidney.

The cysts vary in size from a few centimetres in diameter to a large sac containing a litre or more of fluid. In one case in our series the cyst contained over a litre of fluid. Since the smaller cysts present no symptoms they are not found by the clinician, and only at autopsy.

*Associated Pathology.*—In addition to the cyst, various coexisting pathological lesions may be present. In our series a calculous pyonephrosis was present in two cases and caseous tuberculosis in one case. Cunningham reported a case of coexisting renal calculi and also a case of coexisting hypernephroma. Desno cited a case of a solitary cyst which was present in a tuberculous kidney and O'Neil<sup>23</sup> reported a cyst in a horseshoe kidney.

It is also interesting to note that in Case VIII of our series, in addition to the large solitary cyst found in the kidney, a single cyst three centimetres in diameter, containing clear, serous fluid was found in the liver. This was the only other organ in which a cyst was found.

*Etiology.*—Various theories have been advanced in regard to the etiology of solitary cysts of the kidney. Cunningham<sup>10</sup> states that they are probably due to an obstruction in the uriniferous tubules and to the continued excretion of urine without an outlet.

Kampmeier<sup>2</sup> states that normally the human foetus passes through a period which is characterized by the presence of numerous cystic renal tubules which if they persist and expand at the expense of the adjacent tissue, may cause a renal cyst. Caulk,<sup>9</sup> who studied a large series of these cases, stated that although some cysts may be congenital in origin, it seems evident that the majority are due to obstruction. McKim and Smith<sup>17</sup> believe they may be due to mechanical causes, they may be of neoplastic origin, or they may be congenital.

*Symptomatology.*—Solitary cysts of the kidney do not present any pathognomonic symptoms until they attain sufficient size to produce pressure or until they become palpable. The patient may complain of vague abdominal discomfort, and a sense of fulness, or pain in the region of the kidney. Constipation may be present and urinary symptoms may be entirely absent. Hæmaturia is a rare symptom but it has occurred in cases cited



FIG 10—Röntgenogram showing pressure deformity of stomach and duodenum due to solitary cyst of kidney

by Caulk,<sup>9</sup> Cunningham<sup>10</sup> and O'Neil<sup>23</sup> In our series, hæmaturia was present in one case but this was believed to be due to congestion and enlargement of the prostate. In another case, the patient had had severe attacks of renal colic which were undoubtedly due to the coexisting renal calculi. In a third case marked urinary frequency and dysuria, pyuria and hæmaturia were present but these symptoms were explained by the presence of coexisting renal tuberculosis. Frequently the presence of the tumor is noted by

## SOLITARY CYSTS OF THE KIDNEY

the patient, as in the cases cited by Cunningham,<sup>10</sup> Kretschmer,<sup>21</sup> Blanchard<sup>11</sup> and in one of the cases cited in this paper.

*Diagnosis.*—Often the condition is not diagnosed prior to operation. Bugbee<sup>26</sup> recently made a pre-operative diagnosis of a solitary cyst in the case of palpable tumor of the kidney. The cystoscopic examination and the functional tests gave normal findings. In two of our cases a correct diagnosis was made prior to operation. The presence of hydrops of the gall-bladder, an ovarian cyst or a tumor of the kidney may cause confusion in making a diagnosis. Lesions of the gastro-intestinal tract, however, can be identified by a complete röntgenographic examination, and cholecystography may be used to eliminate the presence of pathological conditions of the gall-bladder.

The röntgenogram may show the outline of the cyst, especially if it arises from the lower pole of the kidney, but cysts of the upper pole are less readily

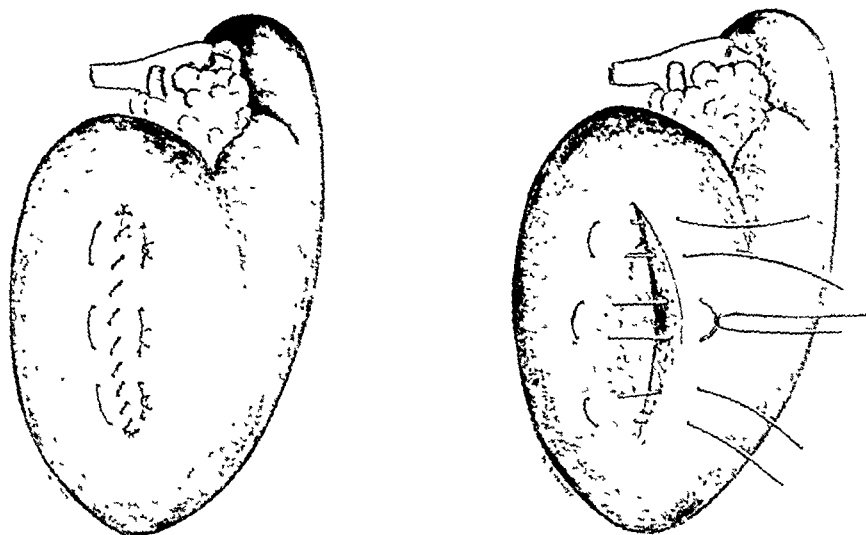


FIG. 11.—Drawing illustrating closure of kidney after removal of cyst.

visualized. The margin of the cyst is continuous with the kidney and there may be a difference in density between the cyst and the kidney. A cyst of the upper pole may attain to such a size that its weight forces the kidney downward, producing ectopia, or the ureter may be displaced from its normal position by the presence of a cyst on the kidney. A gastro-intestinal study may disclose displacement of the colon, stomach or duodenum by the cyst as was noted in one case in this series (Fig. 10).

As the cysts do not communicate with the pelvis or calyces of the kidney the pyelogram may be normal but if the cyst attains sufficient size to bulge into the pelvis a deformity may be shown. The findings from the pyelogram therefore depend upon the size of the cyst, its origin, and the direction in which it grows. In three cases cited by Kretschmer one pyelogram was normal and two were definitely abnormal. Urinalysis and function tests of the kidney usually give normal findings.



*Treatment.*—Conservative renal surgery is especially applicable in the treatment of this pathological condition. The extraperitoneal approach naturally is preferable as adequate exposure can thus be secured. It must be remembered that the wall of the cyst is independent of the kidney capsule although adherent to it. In some cases the cyst can be successfully dissected from the kidney without removing a wedge of kidney tissue, as was accomplished in one case of our series. This is certainly the procedure of choice.

It may be necessary to resect a small wedge of kidney tissue along with the cyst in order to remove all the secreting surface of the cyst (Fig. 11). By an adequate kidney incision an excellent exposure is secured, hæmostasis being controlled by holding the kidney pedicle between the fingers. By releasing pressure upon the pedicle of the kidney spurting blood-vessels may be seen and controlled by catgut sutures. Reapproximation of the wedge-shaped margin of the kidney is accomplished with chromic catgut mattress sutures. Any fatty tissue in the immediate vicinity is then sutured over the incision in the kidney which has been sutured. Nephrectomy should be performed only in the presence of some coexisting pathological condition of the kidney such as a tumor, tuberculosis, or calculi, which has destroyed the renal parenchyma.

#### CONCLUSIONS

1. Solitary cysts of the kidney are of more frequent occurrence than is apparent from the literature.
2. A röntgenogram may reveal the presence of a cyst, especially if it arises from the lower pole of the kidney.
3. Pre-operatively, a pyelogram may show a normal kidney, functional tests may be normal and there may be no urinary symptoms.
4. Conservative renal surgery is the indicated treatment for a solitary cyst, either by dissection of the cyst away from the kidney tissue or by the removal of the cyst together with a small wedge-shaped portion of the pole of the kidney. This will then allow adequate approximation of the kidney tissue.
5. Nephrectomy should be performed only in the presence of some co-existing renal pathological condition, such as a tumor, tuberculosis, or calculi, if deemed advisable.

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## ECTOPIC (PELVIC) KIDNEY

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ECTOPIC or congenitally misplaced kidney although of particular interest to urologists is also a subject of interest to those engaged in general medicine, general surgery, gynæcology and obstetrics. The malposed kidney, especially if it is situated in the true pelvis, is quite prone to disease and the resulting symptoms and signs are apt to be misleading. Pain due to pathological processes in a pelvic kidney is likely to direct attention to other organs. Even if there is a palpable mass in the pelvis the true condition may not be appreciated. Although renal dystopia is considered relatively rare, the condition occurs commonly enough\* to be borne in mind. Frequently ectopic kidneys are poorly or abnormally developed rendering them more likely to pathological states than normal organs. Any of the pathological conditions that occur in the normally situated kidney may be found in the ectopic kidney. It is probable that the chief features of the case reported herewith are typical of the pelvic ectopic kidney with defective ureteral drainage.

CASE HISTORY.—A white woman, aged forty-eight years, was admitted to the Memorial Hospital of Cumberland, Md., April 1, 1930, on account of pain in right lower quadrant of her abdomen. She had been married twenty-four years but never pregnant. Her appendix and gall-bladder had been removed in 1928.

For about fifteen years she had been having pain in the right lower quadrant of her abdomen. Until two years ago this pain was of dull aching character, never severe. It was felt chiefly when she was much on her feet; usually she was relieved by lying down. During the past two years she had suffered with attacks of severe colicky pain in right lower quadrant, radiating to thigh. Nausea, vomiting, prostration, severe pain on top of head, and frequency of urination accompanied the attacks. Morphia was required for relief. At first they occurred at intervals of two to three months, but during the past three months there had been four attacks. Between the attacks there was dull aching pain. Occasionally dull aching pain was felt in left lower quadrant.

Menstrual periods were always irregular, occurring at intervals of fifteen days to three months. The flow has always been scanty. Six months ago the last period occurred.

The patient was of slender build, weight 126 pounds. She appeared comfortable at the time of examination. All teeth had been removed. Tongue was heavily coated. The neck was normal. Thorax had abnormal contour, consisting of a prominent bulging of right lower portion anteriorly. The breasts were small and poorly developed. The heart and lungs were normal. The blood-pressure was 130/75.

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\* H. C. Clark, Eighteenth Annual Report, 1929, p. 274, of the Medical Department, United Fruit Company, stated that among 4215 consecutive autopsies made at the Gorgas Hospital, Canal Zone, a pelvic kidney, either as a unilateral or as a bilateral fused affair, occurred thirteen times. None of them had been recognized clinically.

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An operative scar was in the upper right quadrant. No abnormal masses were felt. The kidneys were not palpable and there was no tenderness in the kidney areas. Apparently there was mild diffuse tenderness in right lower quadrant. Tenderness was most marked at McBurney's point.

Pelvic examination revealed an unusually short vagina and a small, firm, nulliparous cervix. The uterus was small and the adnexa were not enlarged. No abnormal mass was felt.

*Cystoscopic Examination April 1, 1930.*—Except for slight hyperæmia in the trigone the entire bladder had a normal appearance. Both ureteral meati were normal in position and size. In the right ureter a No. 7 catheter passed about half the usual distance between the ureter meatus and the renal pelvis and could not be further introduced. Blood-tinged urine dropped slowly from the catheter. A No. 7 catheter after a little difficulty in the pelvic portion of left ureter passed the usual distance to the kidney and drained clear urine. Indigo-carmin was given intravenously and X-ray examination, including right pyelo-ureterogram was made.

*Right Kidney.*—Specimen discolored with blood, (traumatic—the catheter had been manipulated in the ureter in an effort to pass what seemed to be an obstruction in the ureter); microscopic examination showed high-power field filled with erythrocytes, a few leucocytes. Stained smears revealed no bacteria. There was only a faint trace of indigo-carmin in twenty minutes.

*Left Kidney.*—Specimen clear; centrifuged sediment showed a few epithelial cells. Stained smears revealed no bacteria. There was normal indigo-carmin excretion in twenty minutes.

*Cystoscopic Examination April 5, 1930.*—Catheter No. 7 was passed to left kidney and clear urine drained. Phthalein was given intravenously. The left kidney excreted fifteen per cent. phthalein in fifteen minutes. At the end of the fifteen-minute period a catheter in the bladder removed only a few drops of fluid which contained a faint trace of phthalein, indicating very little function from the right kidney during the fifteen-minute period.

*Röntgen Examination* showed no radiable calculus. The left kidney shadow was large. An outline of the right kidney was not seen on the plain film.

*Right Pyelo-ureterogram* (Fig. 1) (4 cubic centimetres sodium iodide solution used) revealed the right kidney in a median position in the true pelvis, opposite the sacrum. The pelvis, of bifid type, was small. A sharp angulation was present at the ureteropelvic juncture. From the ureteropelvic juncture situated a little to the left of the mid-line the short ureter of small calibre coursed to the right and downward.

*Left Pyelo-ureterogram* showed a large left kidney in the lumbar region—pelvis of kidney opposite the body of third vertebra. The pelvis and calices were moderately dilated. A double kink of ureter was present opposite the fourth lumbar vertebra. At a point just above the vesical portion of ureter there was marked narrowing. Above this the ureter had large calibre.

The attacks of right-sided renal colic were accounted for by the obstruction resulting from the very sharp angulation between the kidney pelvis and ureter. This angulation was probably more acute when patient was in upright position. An extremely short ureter made fixation of the kidney in a higher position impossible. The possibility of overcoming the obstruction at the ureteropelvic juncture by a plastic operation was considered but the small calibre of the ureter and low function of the kidney rendered such a procedure inadvisable. Nephrectomy was therefore advised. May 19, 1930, the patient was again admitted to the hospital and on the following day, under gas-ether anaesthesia, a right rectus incision was made extending from just above the symphysis to a little above the umbilicus into the peritoneal cavity. With the patient in Trendelenburg position, and after packing off the intestines, the right kidney was exposed lying in the hollow of the sacrum. The upper pole was overlying the promontory of sacrum and the inner border of the kidney extended a little to the



Fig. 1—Right pyelo ureterograms 181 A with catheter tip in upper calyx, opposite promontory of sacrum. Note small size of pelvis and calices 181 B Catheter has been removed. Note small calibre of ureter and sharp angulation between pelvis and ureter.

Fig. 2—Left pyelo ureterogram Large kidney, ptosed, pelvis and calices moderately enlarged. Ureter is knicked opposite fourth lumbar vertebra. Stricture area is seen in lower pelvic portion of ureter.

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left of the mid-line. It was noted that the uterus was unusually small and bicornuate. An ovary about the size and shape of a chestnut was found high in the pelvis on the right side. The right Fallopian tube was absent. The left ovary was in normal position and slightly larger than the right. The left Fallopian tube was abnormally long and tortuous.

The peritonæum overlying the kidney was opened transversely and the kidney was readily freed. There was no perirenal fat and a suprarenal body was not seen. One fairly large vessel was found entering the anterior upper portion of kidney. This vessel entered through a cleft separating an upper lobe of kidney from the main portion of the kidney. The chief vessels were found entering the kidney on its mesial and upper aspect. The arteries were derived from the right common iliac.

The ureter, which was of small size, was found inclosed in dense fibrous tissue. This fibrous tissue or fascia seemed to be pulling the ureter toward the left. After

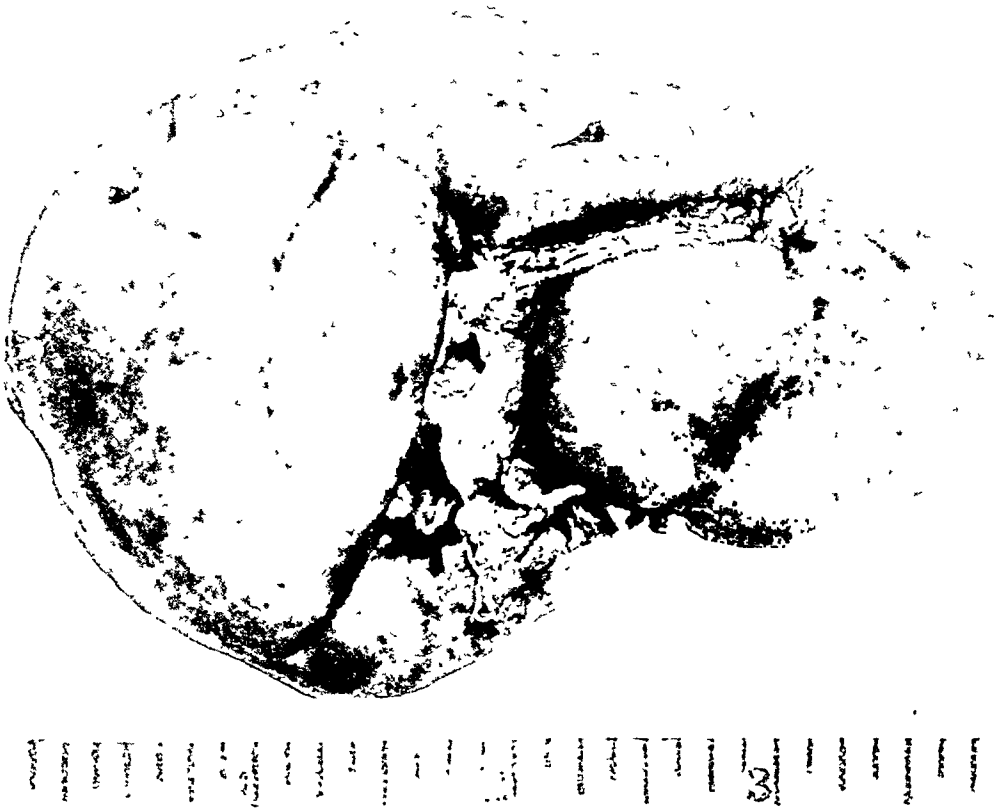


FIG. 3.—Photograph of operative specimen—anterior view. Note the abnormal form of kidney and cleft separating an upper lobe from main portion.

removal of the kidney the posterior peritoneal incision was closed without drainage and the abdominal wall was closed in layers without drainage.

The patient made an uneventful recovery and she was discharged from the hospital June 4, 1930. She has been seen by me four times since then and reported that she was entirely relieved of pain in the abdomen.

*The Specimen.*—The kidney was much smaller than a normal organ. It measured 4 inches by  $2\frac{3}{4}$  inches by 2 inches, weight 108 grams. The shape was abnormal; the lower portion was thicker and wider than the upper portion. On the anterior surface there was a deep cleft separating an upper lobe from the larger main portion of kidney. Near the upper pole on the posterior surface there was a depression to fit the sacrum. The pelvis was small and entirely intrarenal. Sections from the cortical area microscopically showed tubules lined with flattened cells. Fibrous tissue was more abundant than in normal kidney tissue.

*Comment.*—A number of interesting features were presented by this case. The history was rather typical of a patient with chronic renal stasis and attacks of renal colic. Dull pain in the right side of pelvis was clearly due to overdilatation of the right kidney. Acute angulation of the poorly developed ureter produced more or less constant partial obstruction and the attacks of renal colic occurred whenever there was ureteral œdema to increase the obstruction. The increased size of the left kidney was interpreted as compensatory hypertrophy. As a result of a previous inflammatory process there was an infiltration area in left ureter, producing partial obstruction. The kink of left ureter was a result of ptosis and it was regarded as unimportant.

The anomalies of the organs of reproduction consisting of small poorly developed ovaries, absence of right Fallopian tube, infantile bicornuate uterus and abnormally short vagina, accounted for the irregular, scanty menstruation and the sterility. The record of the previous operation does not note the removal of right tube.

Ectopic kidney is to be clearly differentiated from the abnormally movable kidney which has ptosed into the pelvis. The chief characteristics of the ectopic kidney are (1) abnormally short ureter, (2) firm fixation of kidney, (3) blood-vessels derived from the regional vascular trunks.

Failure of the embryonic kidney to reach the usual position results in ectopic kidney. In 5-millimetre embryos the beginning kidney is found as a budding from the caudal end of the Wolffian duct in the sacral region. From this point the kidney grows in a cephalic direction and normally it reaches the permanent renal level opposite the second lumbar vertebra at about the end of the second month. Vascularization of the organ occurs after it has reached its permanent location. If some unknown factor interferes with the upward migration of the kidney it receives its blood supply from the regional vessels as lower aorta, common iliac, internal iliac. The blood-vessels then serve to fix the kidney in its abnormal site. According to Judd and Harrington<sup>1</sup> there is often an associated defective development of Mueller's duct which accounts for the frequent association of genital malformations, particularly in the female. Pelvic organs of the infantile type, absence of a tube or ovary and malformation of the vagina are common associated anomalies. Guizetti<sup>2</sup> states that anomalies of the genitalia can be found in one third of the cases of renal anomalies.

With the present-day extensive use of cystoscopic and X-ray examinations congenital anomalies are being reported with increasing frequency. Dorland<sup>3</sup> in 1911 collected 121 clinical cases of ectopic kidneys from the literature and about 100 had been published since 1898. Huffman<sup>4</sup> states that slight degrees of congenital displacements are not unusual but that marked degrees are rare. He quotes Guizetti and Pariset<sup>5</sup> who reviewed protocols of 20,000 autopsies and found eighteen cases. "Congenital misplacement of the kidney is found about once in 1000 bodies," is the frequency stated in Cabot's "Modern Urology."<sup>6</sup> Collings,<sup>7</sup> who recently reported a case, stated that his

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case was the first recorded in the past twenty years in the record room of Bellevue Hospital. The reported cases indicated that the condition occurs with about equal frequency in the two sexes.

The ectopic kidney may be structurally and functionally normal. Such a kidney may never give rise to symptoms. Frequently, however, the kidney and ureter are malformed and thereby predisposed to disease. Strater<sup>8</sup> reported twelve cases of hydronephrosis and six cases of pyonephrosis in a total of twenty-seven collected cases. Pyelonephritis, calculus, tuberculosis and sarcoma have also been reported. The symptoms, of course, vary with the pathology. When there is ureteral blockage pain is felt in the sacroiliac region and lower abdomen. The pain may vary from mild aching to the severe colic type. Reflex phenomena, particularly gastro-intestinal disturbances and toxic symptoms, are produced when there is renal overdistention and stasis. Increased pelvic pressure incident to pregnancy may severely embarrass a pelvic kidney and if pregnancy goes on to term it is likely that the kidney will interfere with normal delivery and necessitate Cæsarian section.

An exact diagnosis can be made only by urography. The discovery of a mass in the pelvis by rectal or vaginal examination may suggest the diagnosis. Subjecting patients with abdominal symptoms that cannot be diagnosed by ordinary methods of physical and X-ray examination to cystoscopic study will frequently result in a correct diagnosis.

Pyelonephritis and calculus disease are treated by the same methods used for the conditions in normally situated kidneys. Operations that attempt to place the kidney in a more favorable position have been performed without beneficial results. If the ectopic kidney has little or no function and the pathology cannot be relieved by palliative measures nephrectomy is obviously indicated providing there is a healthy, normally functioning kidney on the other side. The pelvic kidney is easily approached by the transperitoneal route.

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## BENIGN TUMORS OF THE BLADDER

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FROM THE CLEVELAND CLINIC

BENIGN, non-papillary tumors of the bladder are of relatively rare occurrence. In a series of cases of benign tumors of the bladder cited by Koll in 1922 only thirty-eight were of this type. Since that time a comparatively small number of additional cases have been cited by Kostjurin, Stevens, McNally, Kidd, Smith and others. Because of the rarity of the condition, it would appear to be of value to offer the following case report, together with a brief review of the literature pertaining to this subject.



FIG. 1.—Fibromyoma of the bladder—gross specimen

CASE REPORT.—A man thirty-nine years of age, entered the Cleveland Clinic complaining of blood in the urine. This condition, which was first noticed two years previously, was accompanied by frequency, urgency, dysuria, and hæmaturia. These symptoms subsided and the patient had felt well until a few months before entering the clinic when he noticed large clots of blood in the urine. During the preceding three weeks blood had been present in the urine each time he voided. At the time the patient presented himself for examination he had nocturia three to five times, voided every hour during the day, and complained of urgency, urethral and vesical pain. He gave an indefinite history of having had bladder discomfort and hæmaturia thirteen years previously. The patient had had a chancre several years before, but otherwise his personal and family history were unimportant. Physical examination elicited definite suprapubic tenderness over the bladder. Laboratory findings were negative except for a four plus Wassermann and the presence of pus and blood in the urine. The cystoscope was passed with ease and 150 cubic centimetres of bloody urine were removed from the

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bladder. Distention of the bladder was difficult on account of irritability. A large tumor with a definite pedicle was found above and lateral to the left ureteral orifice. There was no sloughing. Under spinal anæsthesia the tumor was excised. Convalescence was uneventful and eight months later the patient was free from symptoms.

The specimen consisted of a yellowish-gray tumor weighing thirty grams and measuring 5.5 by 4 by 3.5 centimetres. (Fig. 1.) It was irregular in outline, somewhat round, and had a thin, transparent capsule. On section it appeared to be quite cellular in some portions with a firm, fibrotic central portion leading to a pedicle which was one centimetre in diameter. Parts of the cut surface appeared to be mucoid in character.

Microscopic examination showed the tumor to be covered on the surface by bladder mucosa. The epithelium was of the epidermoid type except for a few gland-like structures below the level of the surface. (Fig. 2.) The rest of the tumor was loose and fibromyxomatous, with numerous small and large spaces showing granular material. There was no evidence of malignancy. The pathological diagnosis was fibromyxoma of the bladder.

*Review of Literature.*—The greater number of benign tumors of the

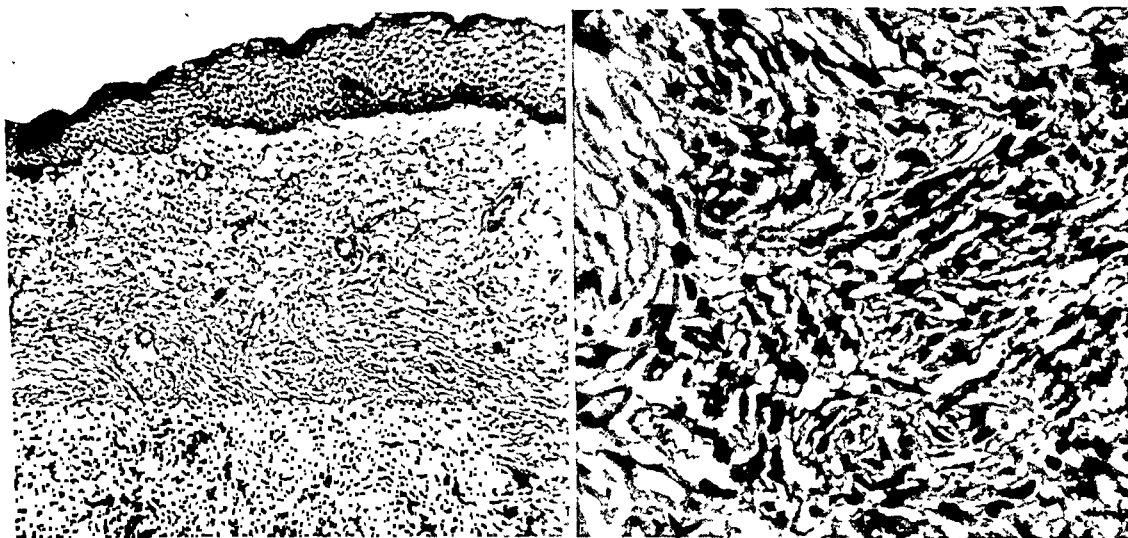


FIG. 2.—Photomicrograph of section of fibromyxoma of the bladder. A— $\times 80$ . B— $\times 400$ .

bladder reported have contained smooth muscle tissue. In Koll's series, this element was present in thirty-four cases; four were cases of fibroma. Since 1922 Maingot, Latzko and Smith have added cases of fibroma, and a case of a fibroma which was successfully removed is cited in this paper.

*Classification.*—Benign, non-papillary tumors of the bladder may be classified as follows:

(1) Myoma: (a) fibromyoma; (b) leiomyoma; (c) rhabdomyoma. (2) Fibroma: (a) fibroma durum (hard fibroma); (b) fibroma molle (soft fibroma). (3) Angioma. (4) Myxoma.

*Histology.*—*Fibroma* arises in the bladder mucosa, and as it enlarges it grows out into the bladder. The *fibroma durum*, as its name implies, is hard, and on examination may or may not be found to be pedunculated. On microscopic examination the bundles of fibres are found to be very closely packed, and very few blood-vessels may be seen, these coursing in a direction parallel with the thick, fibrous bundles. The bundles of connective tissue

fibres vary in thickness, the cells appear to be diminished in number, and the nuclei are scarce. Koll states that *fibromata dura*, or hard tumors of the bladder, may undergo calcification and necrosis on account of their lack of blood supply. In the *fibromata molle*, or soft tumors, the bundles of fibres are more loosely arranged and the nuclei and cells are more abundant. The blood-vessels are more prominent and the tumors, therefore, are more vascular.

*Leiomyomata* are tumors composed chiefly of non-striated or smooth muscle and resemble tumors of the uterus. In the reported cases, leiomyomata have varied in size from that of a pea to that of an egg. They may be single or multiple. Grossly, these tumors consist of dense, firm nodules, which may or may not be pedunculated. The nodules are sharply demarcated from the bladder wall, their consistency depending upon the ratio of muscle elements to the connective tissue. As the tumor extends into the bladder, the nodules carry over them a thin layer of bladder mucosa. Microscopical examination shows these tumors to consist of smooth muscle fibres arranged in interlacing bundles. The stroma consists of connective tissue through which the blood-vessels course.

*Rhabdomyomata* are tumors containing striated muscle, and histologically they are more complex than are other tumors of the bladder. MacCallum cites a case (reported by C. Cones) of a rhabdomyoma in a child, beginning in the vaginal wall and extending into the bladder. These tumors are usually polypoid in character, may be single or multiple, and vary in size from a pea to a large polypus. Microscopical examination shows these tumors to be œdematous, showing small, spindle-shaped cells, among which are scattered larger cells with striated protoplasm. These larger cells are narrow, having a central space which contains many nuclei. The striations are both longitudinal and transverse.

*Angioma* in the bladder resembles angioma found elsewhere in the body. Kelly reports one doubtful case which was observed in 1851. Albarran, in 1892, cited one case of angioma which was found post mortem, another case is cited by R. C. Bryan, and another case has recently been cited by Hamer. O'Crowley and Martland believe that most tumors of the bladder in adults which are described as *myxomyomata* in reality are œdematous fibroblastomata or papillomata with œdema.

*Age Incidence.*—In Koll's collected series of cases of benign tumors of the bladder, one case occurred in the first decade, one in the second decade, nine in the third, five in the fourth, ten in the fifth, five in the sixth, one in the seventh, and two in the eighth decades. The youngest patient reported in the literature (by Sims) was a girl three years of age, with myxofibroma; the oldest was seventy-four years of age. Belfield reports a case of a patient in whom autopsy revealed a myoma of the bladder, and Nauman reports a case of fibromyoma. Very few cases in children are reported because the growth of the tumor is slow, and there may be no symptoms referable to it. This likewise explains the coincidental findings of such tumors at post-mortem examination.

*Etiology.*—The etiology of benign tumors of the bladder is vague. Verhoogen believes they are formed by the development of the partially atrophied Müllerian body. Blume suggests that they may originate from the hypertrophied Müllerian body secondary to a prolonged inflammation. Heger believes they may develop from the hydatid of Morgagni or the lower layer of the utricle. Blume's theory is the most plausible, perhaps, in view of the number of myomata which have been reported. The theories of Verhoogen and Heger do not explain the occurrence of fibroma or angioma. Faye reports a case of fibromyoma found at autopsy in which the tumor was as large as a man's head. Kostjurin cites a case, reported by Kresnetzki, of a myoma which weighed 9,200 grams, and Polaillon cites the case of a fibromyoma weighing 3,200 grams. Riegel reported a case of a myoma which filled the entire bladder. However, the tumors most frequently observed vary in size from that of a pea to several grams in weight.

In most of the cases reported, the tumor has arisen in the region of the ureteral orifice or the trigone, although no part of the bladder is exempt. In a few of the cases cited, the pedicle of the tumor was attached to the vertex of the bladder, and cases of tumors arising from the posterior and lateral walls of the bladder have been reported.

Kidd draws attention to the fact that in benign, non-papillary tumors of the bladder, the main blood-vessels course between the mucosa of the bladder and the tumor, and do not pass directly into the body of the tumor. In this respect they differ from papillomatous tumors of the bladder.

*Symptomatology.*—As a rule, benign tumors of the bladder present no symptoms until they reach a considerable size. For this reason, frequently they are not discovered except at post mortem examination. However, if the tumors have a long pedicle, or if they are near the vesical neck of the bladder, obstructive symptoms may occur which will attract attention to the fact that some pathological condition of the bladder is present. Or the tumor may be in such a position as to cause ureteral obstruction, with subsequent hydronephrosis.

In Koll's cases frequency was present, but not until after the tumor had grown to a considerable size. In one case urinary obstruction was caused by a small, pedunculated tumor; in another, pain over the kidney warranted a complete urological examination which revealed a large tumor which encroached on the ureteral orifice and had produced hydronephrosis. In the case cited in this paper there had been intermittent attacks of hæmaturia with slight irritability of the bladder, for two years.

*Diagnosis.*—The diagnosis of a benign tumor of the bladder can be established by the use of the cystoscope, although in the case of a very large tumor, visualization is difficult, and for this reason prior to operation these tumors are often diagnosed as malignant. In the case of large tumors, the capacity of the bladder is markedly diminished. The cystoscopic appearance of a small tumor is quite different from that of a papilloma or malignant tumor. As a rule, bleeding is not marked, the bladder is less irritable, and the tumor is smooth and glistening. There is, usually, no sloughing, and

touching the tumor with a ureteral catheter does not cause as much bleeding as would be the case if the tumor were malignant.

*Treatment.*—Excision of the tumor is the procedure of choice, a wide excision being made to assure complete removal in case an unsuspected malignant transformation may be present, for although, grossly, the tumor may appear to be benign, microscopic examination may reveal a malignant condition. Recently I saw a case in which a fibromyoma had become malignant.

*Prognosis.*—Removal of the tumor assures a complete cure and an entire cessation of symptoms.

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# LITHOLAPAXY—THE METHOD OF PREFERENCE FOR THE REMOVAL OF VESICAL CALCULI\*

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It is my purpose in this paper to discuss the advantages and disadvantages of the suprapubic removal of stone from the bladder as compared with the crushing operation and evacuation of fragments commonly known as litholapaxy. These two operations alone will be considered since perineal section for stone is seldom employed in the present day unless as part of a perineal prostatectomy.

The incidence of vesical calculus varies in different countries and climates and its proportionate frequency to calculous disease has undergone a radical change with the institution of the thorough urological investigation. For instance, in the early days, before thorough urological and radiological study, stones in the bladder were entirely out of proportion to the number of renal or ureteral stones; Thomson, in India, reported 2962 cases of vesical calculi and only five renal. Joly reports 371 cases of stone in the bladder out of 636 patients admitted to St. Peter's Hospital between the years 1915 and 1924, approximately 50 per cent. of all stone cases admitted to that hospital. In our clinic the proportion between kidney and ureter stones and bladder stones on admission is almost 3 to 1.

The current conception in the treatment of stone in the bladder is that litholapaxy is indicated in all simple stones, that is those without obstruction, without the association of diverticulum, bladder tumor, intense cystitis or urethral stricture, and that surgical removal is always the operation of choice for the complicated stones. Indeed, in the hands of the average surgeon, I am inclined to think that suprapubic cystotomy is more frequently performed even for the simple stone cases. The reason is that litholapaxy is considered a special operation and one to be utilized only by those expert in the manipulation of instruments. From the patient's standpoint, such a practice is not justified and in this paper I will attempt to substantiate the assertion, namely, that litholapaxy, when properly performed, is applicable not only for simple stones but also in a goodly number of stones complicated by other conditions.

Of 225 cases of vesical calculi, the average age was 56.6 years. The frequency according to decades: 1-10, 7 cases; 11-20, 5 cases; 21-30, 11 cases; 31-40, 15 cases; 41-50, 28 cases; 51-60, 43 cases; 61-70, 69 cases; 71-80, 33 cases; 81-90, 6 cases; total of 217 cases in which the age was given. It might be of interest to note that the majority of stones in the bladder occurred between the ages of 40 and 70; the most frequent number

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occurring between 60 and 70, *i.e.*, the age of vesical neck obstruction. There were 197 males or 87.5 per cent. and 28 females, or 12.5 per cent. There were 205 whites, 91.1 per cent. and 20 colored, 8.9 per cent.

A history of previous passage or removal of stone was elicited in forty-five patients or 20 per cent. of the total number. A history of previous renal colics was given by 15.5 per cent., although 60 per cent. of these had not, as far as they were aware of, passed a stone. It was found on admission that 9.4 per cent. of patients with stone in the bladder had associated kidney or ureteral stones but only about half had either previous history of colic, passed a stone, or had a previous operation. In short, about 25 per cent. of the patients had an association either through history or actual finding of upper urinary tract calculus.

In the cases of vesical calculi reviewed there was associated prostatic enlargement in 116 cases, or 51.4 per cent., including twenty carcinomas of the prostate, or 17 per cent.

Stricture of the urethra occurred in seventeen cases, or 7.5 per cent.; of these seven were associated with prostatic hypertrophy.

Other conditions associated with stone were: cancer of bladder, 13; diverticula of bladder, 17; neurogenic bladder, 5; suprapubic fistula, 8; vesicovaginal fistula, 1; recto-urethral fistula, 1; perineal fistula, 2.

In other words, obstruction was present in 55.8 per cent. of all cases. In this obstructive group eighty-eight, or 70 per cent. had given no previous history of stone, such as colics, or passage of calculi, and the X-rays of renal areas were negative on admission; these were obviously cases resulting from obstruction. Thirty-eight cases or 30 per cent. had previous history of colics or calculi.

In the group of non-obstructive cases 55 per cent. gave history either of previous passage of stones, colics, or had stones on admission. Fifty per cent. were associated with cystitis, of which over half were of the incrustated type; whether this is the result or the cause is difficult to determine.

There were eight foreign bodies encountered: one wax-ball, one surgeon's needle, one hairpin, one rubber tissue, two incrustated sutures, two incrustated catheter tips. Only two of the foreign bodies were subjected to open surgery; the wax-ball and the hairpin stones, the others having been extracted endovesically.

Out of the total group of cases 65 per cent. were regarded as good risks and 35 per cent. were poor. Of the poor risks forty-two or 60 per cent. were operated upon by litholapaxy with one death, or 2.4 per cent., sixteen were attacked suprapubically with four deaths, 25 per cent. twelve of the cases were not subjected to surgery due to severe associated conditions such as bad myocardial lesions, pneumonia and central nerve lesions; of these 75 per cent. died during their stay in the hospital without having been subjected to operation.

Of the total number of cases of stone there were 196 operations. In twenty-nine cases no operations were performed, either because they were

extremely bad risks or refused operation. In 112 of the 196 surgical cases litholapaxy was done, or 57.0 per cent.; in thirty-two suprapubic cystotomy alone was done; in fifty-two cystotomy was performed in conjunction with prostatectomy and other surgical procedures such as diverticulectomy, bladder resections for tumor, radium implantation or cauterization. Litholapaxy was performed in forty-four cases in which there was an associated prostatic hypertrophy, seven were done in cases with prostatic carcinoma and eight with strictures of the urethra. In all, over 52 per cent. of the litholapaxies were done in obstructive cases. In sixteen of the obstructive cases in which litholapaxy was performed the cautery punch at a later date relieved the obstruction completely. The association of litholapaxy and minor surgical removal of obstructive conditions at the orifice employing the cautery punch has, in my mind, an increasing field of usefulness. One is apt to misinterpret the extent of prostatic overgrowth in the presence of stone; indeed it is commonly done without such association. Catheter drainage will oftentimes transform the orifice picture so that repeated cystoscopic and rectal examinations prove that the obstructive condition is sufficiently small to be treated without resorting to open surgery.

In the case of stone there is often considerable œdema and reaction around the orifice which rapidly subsides after litholapaxy. It is then found that in many cases no surgical attention to the obstruction is necessary. The same is also true of carcinoma of the prostate in which case the reaction around the carcinoma will frequently disappear under drainage following litholapaxy. I believe that whenever possible one should always shun open surgical attack upon a carcinomatous prostate. The combination of radium implantation and deep X-ray therapy and the punch operation afford much better results than open surgery. In my hands it is rare for the carcinomatous urethra to prohibit litholapaxy.

There have been forty litholapaxies performed on patients who had had previous prostatectomy. In some of these there was evidence of obstruction, others were recurrent stones, in all probability secondary to infection.

It is usually conceded that the presence of a vesical diverticulum contra-indicates any attempt at crushing operation for stone. As a general rule, this is perfectly true. Occasionally such complications, however, occur in very bad risks, usually in older subjects on whom resection of a diverticulum plus prostatic enucleation and the removal of the stone, whether in one or two stages, would be a hazardous procedure and an operation of such magnitude as to be almost prohibitive from the standpoint of safety. In such cases, if the stone be troublesome, it may be crushed and the obstruction relieved by simpler transurethral measures. In the seventeen cases of diverticula which have occurred in this series, six were treated by litholapaxy either alone or with the cautery punch operation with no mortality. Nine resections of the diverticulum were performed with prostatectomy later, with one death, or 11 per cent. mortality. In two cases no operation was performed, one had an aneurism, the other pneumonia.



I am perfectly willing, in a bad risk and even in some fairly good risks, providing the diverticulum is not too large and is draining fairly well, to be content with the relief of obstruction at the orifice and the crushing of the stone. Occasionally, the penalty of such conservative procedure may be that fragments will fall into the diverticulum and there produce larger stones.

Of the thirteen carcinomas of the bladder in this series, eight were not associated with obstruction, whereas the other five were. Litholapaxy was performed in five instances; small stones were removed with the cystoscopic rongeur in two others. Carcinoma of the bladder is regarded as an absolute contraindication to litholapaxy; most surgeons agree that the bladder should be exposed and the carcinoma treated by open operation of one type or another. I am, however, strongly opposed to open bladder surgery in the treatment of most cases of bladder carcinoma. After a lengthy experience with this type of surgery I have abandoned it and have been more than gratified with the results obtained by repeated radium implantations and diathermy through the cystoscope in association with deep X-ray therapy.

The crushing of the stone in the presence of carcinoma does not appear to present any extreme hazard. After being seized, the stone is crushed, not on the bladder wall, but in its cavity. On the contrary, the danger of rupture should be very slight and the danger of spread of the tumor should be much less than that occasioned by open surgery.

There were twenty-seven cases of intense severe cystitis in this series, another supposed contraindication to litholapaxy. This fact is mentioned in order to make impressive what can be accomplished by adequate pre-operative drainage and the proper anæsthesia. Bladder irritability and contracture are minimized and with twilight and caudal anæsthesia I have experienced no trouble with this complication. Fifteen of these twenty-seven cases were operated upon by litholapaxy after catheter drainage and preparation without mortality or serious complications. Indeed, intense cystitis is much less to be feared than a less severe pyelonephritis.

There is no doubt that litholapaxy is the ideal procedure for simple uncomplicated stones in the bladder. The simplicity of the operation without general anæsthesia, its freedom from complications with consequent short hospitalization, often amounting to only one or two days, and freedom from economic loss stamp this operation unquestionably as the one of choice in this type of stone. I am thoroughly convinced, however, that it has also an ever-increasing field of usefulness in the complicated cases and should be more frequently employed. In a great measure the same complimentary remarks may be directed here as in the simple stones.

Concerning the size and multiplicity of calculi, with reference to their suitability to litholapaxy, I have records of 169 cases in this series where the size and number of stones were mentioned. Of these sixty-six were multiple, or 39 per cent., of which 60 per cent. were cured by litholapaxy; fourteen, or 35 per cent., requiring multiple-stage operations. There were

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eighty-two large stones either alone or associated with smaller ones. Twenty-seven of these were cured by litholapaxy, or 33 per cent. Of these, eight cases were done in multiple stages, or 29.6 per cent. Multiple operations were performed in the entire group in one-third of the cases. In the small stones litholapaxy was performed in multiple stages in 35.4 per cent. It is thus seen that the size of the stone or the multiplicity does not necessarily influence the number of operations required to effect a cure. Other things, such as the patient's tolerance, the character of the stone, associated lesions in the bladder, kidney and urethra enter into the picture.

One of the most difficult stones to crush was a small stone no larger than a cherry. It proved to be a xanthine stone, the only one in the series. The size of the stone, *per se*, within certain reasonable limits, offers no contraindication to stone crushing. Very often the larger the stone the softer and the easier it is to crush. Some of the largest stones have been the easiest to cure by litholapaxy.

In one case the patient had had a suprapubic prostatectomy for carcinoma a year prior. We found he had a very close stricture of the urethra and there was great difficulty in passing a filiform, but it was finally dilated to a No. 20 French. The stone in his bladder which was detected by X-ray was over 2 inches in diameter. After repeated attempts at dilatation of the urethra it was found impossible to dilate it sufficiently to investigate the bladder cystoscopically or to attempt any other urethral manipulations. When a low spinal anæsthesia was given there followed a most striking relaxation of the urethra, so that in spite of his carcinoma, a lithotrite was easily inserted and the large stone was crushed in one sitting. I am positive nothing short of spinal anæsthesia could have produced sufficient relaxation to have permitted litholapaxy. This patient had previously been given general and caudal anæsthesia in an attempt to dilate the urethra.

This suggests a possible contraindication to litholapaxy, namely, bladder contracture and stricture of the urethra. One is often misled in the interpretation of the amount of contracture, both in urethra and bladder, by muscle spasm. The relaxation produced by means of caudal or spinal anæsthesia enables the true capacity to be determined and many patients may be spared a major operation who would otherwise have been subjected to it. Contracture of the bladder, often regarded as a contraindication to litholapaxy, is in a great majority of instances physiological. True contracture seldom exists except in tuberculosis and carcinoma of bladder and occasionally in calculi associated with general vesical wall infiltration, and pericystitis.

As to the technic of litholapaxy. In the first place, proper anæsthesia is essential. In many of the simple cases local urethral anæsthetic is all that is necessary. The majority, however, do much better under caudal and twilight. There appears to be no necessity for a general anæsthetic.

In certain rare cases spinal is the ideal anæsthetic. The chief structures to be protected during this operation are the urethra and bladder wall. It is essential to crush as much as possible during one introduction of the

lithotrite and then remove it for evacuation. It is seldom necessary to insert the lithotrite more than twice at one sitting. There is one procedure which is very important in protecting the urethra from tears or injury resulting from fragments adhering to the instrument. Before it is withdrawn it is advanced into the bladder and when it is centred in the open bladder, the male and female blades are jammed together in order to throw off the impacted fragments and then screwed together tightly before extraction.

I much prefer to do repeated litholapaxies, possibly a week apart, than to do too much at one sitting.

The bladder should suffer very little trauma as one should always depress the jaws of the lithotrite toward the base of the bladder and after opening and grasping the calculus they are firmly locked and centred in the open bladder away from the wall before crushing is commenced. Employing this technic it is very often possible to crush a stone of considerable size with very little bleeding.

In very large stones, even those that are too large to be completely grasped by the instrument, I have found it advantageous to crack the outer coating, grasping them laterally. On several occasions I have done this without evacuation and by changing the chemistry of the urine by injections of bulgara bacillus, the stone readily passed into solution and disappeared, or had undergone spontaneous fragmentation making litholapaxy a simple procedure for the removal of the remaining fragments.

It is my custom always to follow litholapaxy by instillations of bulgar bacilli with very gratifying results. On several occasions I have observed the bladder cystoscopically after crushing and found numerous fragments in the bladder and a week later have found the bladder entirely clean. This is particularly true in the phosphatic stones. Where repeated crushings are required an indwelling catheter is employed and careful attention given to the bladder.

History shows that the first lithotroties were done in multiple stages on account of fear. Recently an endeavor has been made to do the operation in one stage, usually under general anæsthesia. I feel that the repeated operation on difficult stones, whether large or small, or multiple, is far preferable to a long-continued operation under anæsthesia and to the excessive trauma from repeated instrumentations. One usually has to wait four or five days to a week between operations until the reaction from the first is over.

I have seen only one serious complication following multiple-stage litholapaxy and this resulted from the patient's lack of coöperation and was not the result of the operation itself. Four days after a simple litholapaxy, the patient left the hospital, under protest, with an indwelling catheter. He promised to return in a few days, but did not return for ten days. In the meantime he removed his catheter, was able to void without difficulty for the next twenty-four hours and then suddenly had retention due to a frag-

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ment which became impacted in the urethra at the peno-scrotal juncture. He was finally able to urinate but did not pass the fragment. About a week later he appeared with a large peri-urethral abscess at the root of the penis on the dorsum. It ruptured spontaneously and a spicule of stone was projecting from the dorsum of the penis. This left a large, fistulous opening which persisted for sometime, but when I last saw him it had practically cleared. The remaining fragments were later crushed and the bladder entirely healed. This complication would not have happened if the patient had been under supervision. It is always essential to cystoscope the patient after litholapaxy before discharge to be sure that all fragments have been removed.

There have been but very few complications from litholapaxy in these cases: pyelonephritis, 4.4 per cent.; epididymitis, 4.4 per cent.; hæmorrhage, once; peri-urethral abscess, 3 per cent.; impacted calculus of urethra, 3 per cent.

The average duration in the hospital in 112 cases of litholapaxy has been ten days. Most of the simple stone cases were out in two or three days. Hospitalization was lengthened by the complicated cases which really remained in for the treatment of the complications, such as hypertrophy, tumor and infection.

The indications for the suprapubic operation are large stones, stones which are adherent to the bladder wall and those associated with other pathological conditions, such as prostatic obstruction, stricture, diverticulum, or tumor. The average stay in the hospital from suprapubic cystotomy has been thirty-nine days.

The mortality from simple cystotomy in thirty-two cases was one death, 3.1 per cent. In the fifty-two cystotomies for stone in which prostatectomy or prostatectomy with resection of the bladder for tumor or for diverticulum was done, there were seven deaths, or 13.4 per cent. In this group four deaths followed bladder-wall resection along with prostatectomy and stone removal. Disregarding these, the mortality from prostatectomy and stone has been 6.2 per cent. This has occurred in the face of the most accurate care in preparation, anæsthesia, surgery and treatment. However, it follows the trend of general mortality rate throughout the world; for instance, in St. Peter's Hospital, London, from 1915 to 1924, the mortality rate from suprapubic cystotomy was 9 per cent. according to Joly, and Freyer reported 14.6 per cent. in 116 cases of suprapubic lithotomy. Watson showed 13.2 per cent. in combined statistics of over 3000 suprapubic lithotomies. It is thus evident that the mortality rate following this operation is exceedingly high.

Of the 112 cases of litholapaxy there was one death, or 8/10 of 1 per cent. This individual was a bad risk; he was uræmic, had severe myocardial change, reacted badly from instrumentation, developed epididymitis, abscess of the testicle, septicæmia and died.

## JOHN ROBERTS CAULK

St. Peter's Hospital for stone mortality, litholapaxy, 226 cases—2.2 per cent.

Freyer Hospital for stone mortality, litholapaxy, 986 cases—2.5 per cent.

Watson and Cunningham Hospital for stone mortality, litholapaxy, 17,736 cases—2.4 per cent.

It thus seems that the average mortality in litholapaxies is around 2 per cent.

The data with reference to comparative recurrence of stone from the two operations are not sufficient to draw definite conclusions. I have been able to follow a large proportion of litholapaxies and find recurrence in 7.1 per cent. of cases. The returns on the open surgery were so few in number that no definite information can be furnished. There were forty patients in the group of litholapaxies who had had previous suprapubic or perineal operations. It does appear definite that recurrences following litholapaxies are less frequent than with cystotomy.

In conclusion it may be stated that:

1. Litholapaxy appears to be the operation of choice in the majority of stones in the bladder regardless of size or multiplicity.

2. The stone, *per se*, seldom contraindicates its operation and when associated with other conditions such as obstruction, tumor, diverticulum or active cystitis, it may lend itself to litholapaxy in a very definite percentage of cases.

3. It is strikingly free from complications and its mortality rate is relatively insignificant.

4. Compared to open surgery, the results gauged by the frequency of recurrence seem to be superior.

5. In this day of demand for efficiency with minimum sacrifice of time, in point of economic loss occasioned by lengthy hospitalization following open operation, litholapaxy offers a ready avenue of escape.

# ANALYSIS OF SEVEN HUNDRED CONSECUTIVE APPENDECTOMIES

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THOUSANDS of articles have been written on the subject of appendicitis, and all phases have been studiously covered. Further studies, however, should be made as the incidence of appendicitis seems to be increasing, and the mortality rate does not show any noticeable improvement. Appendicitis is steadily increasing in frequency. The rate has advanced from 11 per 100,000 in 1920, to 14.4 per 100,000 in 1925; according to a governmental report on vital statistics, 20,000 people in the United States die annually from appendicitis.

The following report is based on the records of 700 consecutive cases of appendicitis operated upon at the University Hospital from January 1, 1920, to January 15, 1929.

*Sex*—There was an almost equal distribution of cases between the sexes: 354, or 50.5 per cent., were males, and 346, or 49.5 per cent., were females. There seems to be an increased incidence in males over females especially when large series of cases are studied. Those that show a majority on the female side usually deal with a larger number of the so-called chronic cases and also often include appendices that have been removed during gynecological operations.

When the cases are divided into the acute and into the chronic or interval groups, we find that there are 60.9 per cent. males and only 39.1 per cent. females in the acute group. The exact reverse is true in the chronic or interval cases with 61.4 per cent. females and 38.6 per cent. males.

*Age*—Acute appendicitis is primarily a disease of adolescent and early adult life. Exactly 75 per cent. of the cases developed during the second and third decades. (See Fig. 1.) Barkley found a majority of cases to fall between the ages of fourteen and forty-five. Bar found 65 per cent. between eleven and thirty; Richardson, 50 per cent. between fourteen and forty-five; Seifert, 67 per cent. between eleven and thirty; and Denk and Hoffman report the peak incidence during the second and third decades.

The average age was 21.9 years. This is somewhat lower than MacCarty's figures of 23.5 years and Burgess' of 26.3 years.

*Seasonal incidence*—The highest incidence of appendicitis is found during the summer season. Why this should be true is difficult to explain. Possibly it is due to the increased prevalence of gastro-intestinal disorders at this time of the year.

*Previous infections*.—Forty-one, or 5.8 per cent., of all the cases gave

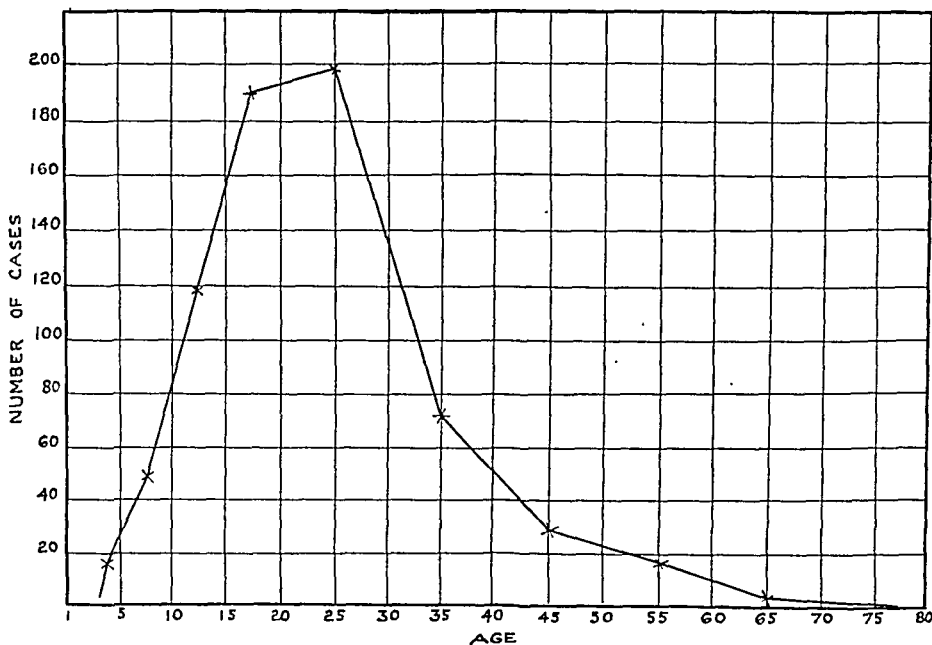


FIG. 1.—Distribution of cases according to age.

a definite history of recent infection, the most common of which were severe colds, sore throats, and tonsillitis. There were also two cases of measles, one of mumps, one of whooping cough, and one of scarlet fever. The presence of recent or simultaneous infection was found

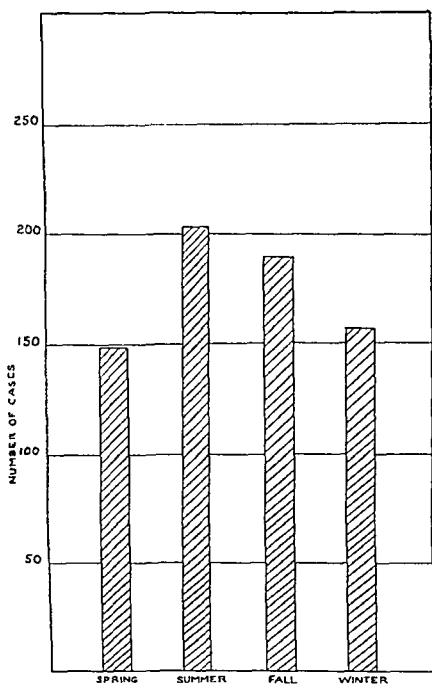


FIG. 2.—Distribution of cases according to seasons.

to be most prevalent among children, that is, in 31 per cent. of the cases. Brenne-mann found sore throats present in 17 per cent. of the children he operated upon for acute appendicitis, while Richter reported 4.0 per cent. in 172 cases. Evans stated that among the students at the University of Wisconsin acute appendicitis came in epidemics and that 86 per cent. showed "demonstrable primary upper respiratory tract infection."

It is exceedingly difficult at times, but very important, to differentiate between the abdominal symptoms due only to severe upper respiratory or pulmonary infection and those due to an acute appendicitis accompanied by such an infection.

*Previous attacks.*—More than one-half, or 57.1 per cent., of the patients gave a definite history of one or more previous attacks; 8.8 per cent. gave a negative history, while on 35 per cent. of the records no mention of the matter

## SEVEN HUNDRED APPENDECTOMIES

was made. This high figure is due partly to the fact that a great many of our patients were sent into the hospital as interval cases. Dowden reports 37 per cent. previous attacks; Carson, 35 per cent.; Isaacs, 30 per cent.; Burgess, 28.4 per cent.; and Backman, only 25 per cent.

*Classification of cases.*—An attempt has been made to classify the cases into separate clinical, surgical, and pathological groups. This was quite difficult to do and far from satisfactory in all instances. The purpose in mind was to see if one could predict correctly the surgical and pathological findings from clinical and laboratory information.

*Clinical groupings.*—*I. Mild.*—In this group were included those patients who complained of abdominal pain, usually located in the right lower quadrant, with loss of appetite and some nausea. The abdominal findings included tenderness over or near McBurney's point with very little or no muscle spasm on palpation over this region.

*2. Moderate or severe.*—These people complained of more pain with flexion protection of the abdomen, of anorexia, and of nausea or vomiting. There was usually marked tenderness present both on abdominal and rectal examination, with rigidity of the muscles and often rebound tenderness. The latter sign is almost conclusive proof of peritoneal involvement.

*3. Very severe.*—This division included those cases considered practically moribund with cold, clammy skin, anxious facies, dehydration, fecal vomiting, distention, and other signs of peritonitis and impending death.

*Pathological groupings.*—Every appendix removed at the University Hospital is examined grossly and microscopically by the pathologist. Unfortunately, eighteen of the pathological records have not been completed or have been lost. In eight cases the appendix was not removed. In 682 cases, the findings recorded permit of the following evaluation:

1. No evidence of active inflammation.
2. Acute recurrent appendicitis with previous infection evidenced by the presence of perivascular collections of lymphocytes in the serosa.
3. Acute suppurative appendicitis.
4. The so-called "obliterative" appendix.

The most satisfactory classification was found to be the surgical-pathological. The cases were grouped into five classes and each will be discussed separately.

*1. Chronic appendicitis.*—In this group were included all cases that came into the hospital with a definite history of previous attacks of appendicitis. Among them were many cases which should be classified as subacute or as acute subsiding appendicitis, since on admission to the hospital they showed definite tenderness over McBurney's point. There were also included a few cases that did not give a good history for recurrent appendicitis, but nevertheless were operated upon after all other possible lesions and especially kidney colic or pelvic infection had been ruled out by careful examination. Such operations were performed because these patients were sent to us by their doctors with the diagnosis of acute appendicitis, and we felt that we were not



justified to send them back into the country without considering the diagnosis submitted, especially as the doctors had usually seen the patients during attacks.

There were 339 so-called interval cases. This number, in proportion to the entire series, is large. Fully 90 per cent. of our patients come from rural communities and often from the very "back-woods" itself. As a result many cannot be moved at the time of their primary attack and are sent in later after the inflammation has subsided. There was one death in this series, or a mortality of 0.3 per cent. The average leucocyte count was low, 8,000, with an average polymorphonuclear count of 67 per cent. Seventy-seven per cent. of the cases, or 257, gave a definite history of one or more previous attacks, usually mild in character. Out of 321 specimens reported, 61 per cent., or 203, showed no sign of any inflammation present; 32 per cent., or 104, showed signs of recent inflammation; 3 per cent., or 11, showed an obliteration of the lumen of the appendix, and 3 per cent., or 9, showed actual suppuration. The mortality rate of 0.3 per cent. fits well with other reports. It should be 0 per cent., however, and any death must be attributed to a slip in technic at some stage during the operative procedure or to some unusual complication. The cause of death in this case was probably due to a long exploratory procedure in a very obese middle-aged individual. The appendix was finally found under the liver attached to a cæcum which had not descended normally. The patient died as a result of a severe paralytic ileus.

*Acute appendicitis.*—There were 361 cases of acute appendicitis. This does not include many so-called subacute cases which have been placed with the interval group. The mortality rate for the acute cases was 6.4 per cent. Very few statistics could be found that definitely separated the acute cases from the others when giving mortality rates.

2. *Acute suppurative appendicitis.*—There were seventy-two cases in this group. Included are all cases of suppuration of the appendix where there was no peritoneal involvement or abscess formation. There was one death with a mortality of 1.4 per cent. The average leucocyte count was 13,600, with an average polymorphonuclear count of 78.3 per cent. Two-thirds of the cases were classified clinically as moderately severe and one-third as mild. Sixty-five per cent., or 47 specimens, showed suppuration microscopically in all of the coats of the appendix, while in 28 per cent., or 20, there were signs of inflammation present only in the serosal portion; in five cases there was no record of the pathologist's findings, but the gross description by the surgeon of the appendix in each case definitely placed it in this group.

3. *Acute appendicitis with local peritonitis.*—In this group were 156 cases with four deaths, or a 2.5 per cent. mortality. The average leucocyte count was 14,800 with an average polymorphonuclear count of 87.4 per cent. Eighty-four per cent. of the cases gave a history of moderately severe symptoms with corresponding physical findings; the remainder were mild. Microscopic examination revealed suppuration in 87 per cent. of the cases examined,

# SEVEN HUNDRED APPENDECTOMIES

and acute recurrent appendicitis in 13 per cent. In one case there was no report found.

4. *Acute appendicitis with abscess.*—In this group were included all cases of suppurative appendicitis with abscess formation. Out of 112 cases there were eleven deaths, or a mortality of 9.7 per cent. Eighty-four of the abscesses were localized to the immediate neighborhood of the involved appendix; while in twenty-nine the collections of pus were elsewhere—four in the subphrenic region and the remainder in the flank or pelvis. The average leucocyte count for the entire group was 18,000 with an average polymorphonuclear count of 80.1 per cent. Nearly all, or 87 per cent., had moderate or severe symptoms and findings. The pathological report on 92 per cent. of the cases showed suppuration. Two per cent. showed acute recurrent appendicitis; in seven cases the abscess was drained without removing the appendix.

5. *Acute appendicitis with diffuse peritonitis.*—This group included all cases of suppurative appendicitis with diffuse peritonitis usually of streptococcic origin. There were twenty-one cases with eight deaths, or a mortality of 38.0 per cent. The average leucocyte count was 19,000 with an average polymorphonuclear count of 84.3 per cent. All of the cases were classified as having had moderate or severe symptoms and findings. Four cases were practically moribund when they arrived at the hospital. All of the appendices removed showed suppuration when examined under the microscope. In one case the appendix was not removed, although the peritoneal cavity was drained.

TABLE I summarizes the pathological findings according to surgical groupings.

TABLE I  
*Microscopical Pathology*

| Type of appendicitis                                | No. of cases | Serosa only | Suppuration | Obliterative | Normal | No record | Appendix not removed | Per cent. mortality |
|---|--------------|-------------|-------------|--------------|--------|-----------|----------------------|---------------------|
| Interval or chronic. . . . .                        | 339          | 104         | 9           | 11           | 203    | 12        | 0                    | 0.3                 |
| Acute suppurative. . . . .                          | 72           | 20          | 47          | 0            | 0      | 5         | 0                    | 1.4                 |
| Acute suppurative with local peritonitis. . . . .   | 156          | 19          | 136         | 0            | 0      | 1         | 0                    | 2.5                 |
| Acute suppurative with abscess. . . . .             | 112          | 2           | 103         | 0            | 0      | 0         | 7                    | 9.7                 |
| Acute suppurative with diffuse peritonitis. . . . . | 21           | 0           | 20          | 0            | 0      | 0         | 1                    | 38.0                |
| Totals. . . . .                                     | 700          | 145         | 315         | 11           | 203    | 18        | 8                    | 3.4*                |

\* Average.

*Clinical findings.*—When one considers only the symptoms and the physical examination of each case, the clinical picture is not always an exact index of the severity of the infection present in the appendix and surrounding peritoneum. In a large proportion of cases, however, one can prophesy with a

fair degree of certainty the surgical findings and the prognosis for each case. In the uncomplicated cases of acute appendicitis, 80 per cent. were classified as mild or only moderately severe, while the remainder, 20 per cent., were considered severe. In the cases with abscess formation, a much smaller proportion showed only mild symptoms, about 13 per cent., while the other 87 per cent. were severe. In this latter group were included three cases in a moribund condition when admitted. In cases with local peritonitis 84 per cent. gave histories suggesting a severe process, while only 16 per cent. were considered mild. Where there was diffuse peritonitis no mild cases were recorded and more than a half of such cases were classified as severe with four considered moribund. Generally, therefore, the clinical findings are in agreement with the severity of the surgical condition.

When we analyze the cases that died, it would seem that the clinical findings are of less value in making a prognosis on a case than they are in determining the surgical condition. Out of the twenty-four deaths, one was considered as mild on admission, six as only moderately severe, fourteen as severe, and three as moribund. One patient died as a result of an interval operation.

As it is impossible to determine the exact surgical condition present and the final outcome of the case from the clinical findings, procrastination should always be avoided and immediate appendectomy carried out.

*Time factor.*—The number of hours between the onset of symptoms and the time of operation is important. The average time for the 228 cases with the disease localized to the appendix and neighboring peritoneum was thirty-six hours, while eighty-six hours had elapsed in the cases with abscess formation. However, the average time for the cases with diffuse peritonitis was sixty-one hours—less than that for abscess formation. Those with peritonitis were brought to the hospital somewhat sooner, probably because the symptoms were more rapidly progressive in severity, whereas in those cases with abscess formation there was often a definite history of relief for a number of hours

TABLE II  
*Leucocyte Count*

| Appendicitis                     | Leucocytes |         |        | Polymorphonuclears (per cent.) |         |        |
|----------------------------------|------------|---------|--------|--------------------------------|---------|--------|
|                                  | Average    | Highest | Lowest | Average                        | Highest | Lowest |
| 1. Interval.....                 | 8,000      | 9,000   | 5,000  | 67.6                           | 96.0    | 33.0   |
| 2. Suppurative.....              | 13,600     | 29,000  | 7,000  | 78.3                           | 93.0    | 50.0   |
| 3. —with local peritonitis.....  | 14,800     | 30,000  | 3,000  | 87.4                           | 96.0    | 52.0   |
| 4. —with abscess.....            | 18,000     | 48,000  | 4,000  | 80.1                           | 95.0    | 32.0   |
| 5. —with diffuse peritonitis.... | 19,000     | 42,000  | 5,000  | 84.3                           | 94.0    | 32.0   |

with a later relapse. Marsch reviewed 9000 cases and found that the mortality rate for those patients operated upon during the first twenty-four hours

# SEVEN HUNDRED APPENDECTOMIES

was 1.1 per cent., for the second twenty-four hours 1.8 per cent., for the third, 4.8 per cent. and for those of four days or over 11.7 per cent.

Generally the degree of leucocytosis indicates the amount of body resistance, and the degree of neutrophil increase the severity of the inflammatory process. A low count may mean a mild infection, a walled-off abscess with cessation of absorption of the exudate, or poor body resistance. Three cases in this series died with leucocyte counts of 3,600, 3,900, and 4,950 respectively. The polymorphonuclear count is a fairly accurate indication of the severity of the infection. From the above table it would seem that peritoneal inflammation gives a higher count than does the presence of pus walled off in an abscess. In two cases that died with abscess formation the counts were 32 per cent. and 59 per cent. respectively. Both these cases had leucocyte counts of less than 5,000.

TABLE III  
*Temperature and Pulse Rate on Admission to Hospital*

| Appendicitis                      | Temperature |      |      |      |      | Pulse rate |        |     |     |
|-----------------------------------|-------------|------|------|------|------|------------|--------|-----|-----|
|                                   | 99°         | 100° | 101° | 102° | 103° | 90         | 99-110 | 120 | 130 |
| 1. Interval.....                  | 294         | 33   | 8    | 3    | 1    | 292        | 38     | 8   | 1   |
| 2. Suppurative.....               | 33          | 31   | 4    | 4    | 0    | 43         | 25     | 3   | 1   |
| 3. —with local peritonitis.....   | 63          | 56   | 22   | 13   | 2    | 91         | 44     | 18  | 3   |
| 4. —with abscess.....             | 37          | 23   | 23   | 20   | 9    | 36         | 45     | 24  | 7   |
| 5. —with diffuse peritonitis..... | 1           | 3    | 3    | 5    | 9    | 2          | 4      | 7   | 8   |

As one would expect, the temperature and pulse rate rise proportionately to the severity of the disease. However, appendicitis is seldom accompanied by a high temperature. Only 16 per cent. of the acute cases had a fever of more than 101° and only 5.6 per cent. of more than 102°.

*Rectal examination.*—In the interval cases there were 117 rectal examinations noted with sixty-seven negative findings; forty-nine showed some tenderness on the right side. In the acute suppurative cases fifteen examinations were negative, twenty-five showed tenderness on the right, and in three a mass was palpated. Where local peritonitis was present, nineteen examinations were negative and sixty showed tenderness, while in two instances a mass was felt. In the abscess cases twenty-eight showed tenderness against twenty-five negative examinations and in ten cases a mass was present. The cases with diffuse peritonitis showed the highest proportion of rectal tenderness, being thirteen out of the fourteen examinations recorded.

*Urine examination.*—The urine was examined in each case before operation was performed. Any case showing pus- or red blood-cells with an indefinite history for appendicitis or a history suggestive of a urinary disorder was studied further. An X-ray examination of the urinary tract and a cystoscopic examination was made whenever it was thought necessary to determine the presence or absence of calculi. That pus- red blood-cells, and

cases are often present in the urine coincident with acute appendicitis is shown in the table below. There was one case with gross hæmaturia. Probably the presence of pus- or red blood-cells is due to one of the four following conditions: (1) Action of toxins on the kidney by way of the blood-stream; (2) direct involvement of the kidney itself by extension of an abscess upwards and retroperitoneally; (3) creation of an ureteritis by an inflamed appendix lying in contact with the ureter; and (4) inflammation of the bladder due to an appendiceal abscess in the pelvis, especially when the bladder forms part of the abscess wall.

TABLE IV

| Appendicitis                      | Pus | Red blood-cells | Red and white blood-cells | Red and white blood-cells casts |
|-----------------------------------|-----|-----------------|---------------------------|---------------------------------|
| 1. Interval.....                  | 0   | 0               | 0                         | 0                               |
| 2. Suppurative.....               | 2   | 1               | 3                         | 0                               |
| 3. —with local peritonitis.....   | 5   | 5               | 3                         | 1                               |
| 4. —with abscess.....             | 5   | 0               | 3                         | 0                               |
| 5. —with diffuse peritonitis..... | 2   | 0               | 3                         | 1                               |

In Table V are summarized some of the clinical findings according to different surgical-pathological groupings.

TABLE V  
*Analysis of Seven Hundred Appendectomies*

| Type of appendicitis       | No. of cases | Average white blood-cells | Average poly-nuclears (per cent.) | Temperature over 101° (per cent.) | Pulse over 120 (per cent.) | Abnormal urine (per cent.) | Mortality (per cent.) |
|----------------------------|--------------|---------------------------|-----------------------------------|-----------------------------------|----------------------------|----------------------------|-----------------------|
| Interval or chronic.....   | 339          | 8,000                     | 67                                | 3                                 | 3                          | 0                          | 0.3                   |
| Acute suppurative.....     | 72           | 13,000                    | 78                                | 6                                 | 6                          | 7                          | 1.4                   |
| —with local peritonitis... | 156          | 14,000                    | 87                                | 10                                | 12                         | 9                          | 2.5                   |
| —with abscess.....         | 112          | 18,000                    | 80                                | 26                                | 30                         | 8                          | 9.7                   |
| —with diffuse peritonitis. | 21           | 19,000                    | 84                                | 70                                | 75                         | 30                         | 38.0                  |

*Mortality.*—Out of the 700 cases there were twenty-four deaths, or a 3.4 per cent. mortality. It is regrettable that the rate should be as high as this. Unfortunately, however, the patient, and too often the doctor, procrastinate too long and the disease ceases to be confined to the appendix.

Six hundred thirty-six out of the 700 operations were performed by ten men who were or are still serving their Fellowships in Surgery. The remaining sixty-four were performed by five Senior attending surgeons.

Nearly all of patients were transported by automobile or train many miles from all parts of the state before they arrived at the hospital. Cases with signs of rapidly spreading peritonitis and those in very poor condition are probably best treated expectantly for a few days until they are in better

## SEVEN HUNDRED APPENDECTOMIES

condition to stand operation. Formerly it was rule at the University Hospital to operate immediately on all cases of acute appendicitis, unless they were in a moribund condition. Lately, however, when the diagnosis of diffuse peritonitis is definite, we wait until that process has had an opportunity to localize itself.

The following general principles have been carried out in nearly all of the cases. No matter what the hour, as soon as the diagnosis of acute appendicitis has been established, operation was performed. Appendectomy was always done unless the appendix could not be found readily in an abscess wall. Out of the 113 cases with abscess, the appendix was not removed seven times. On discharge from the hospital these patients were instructed to

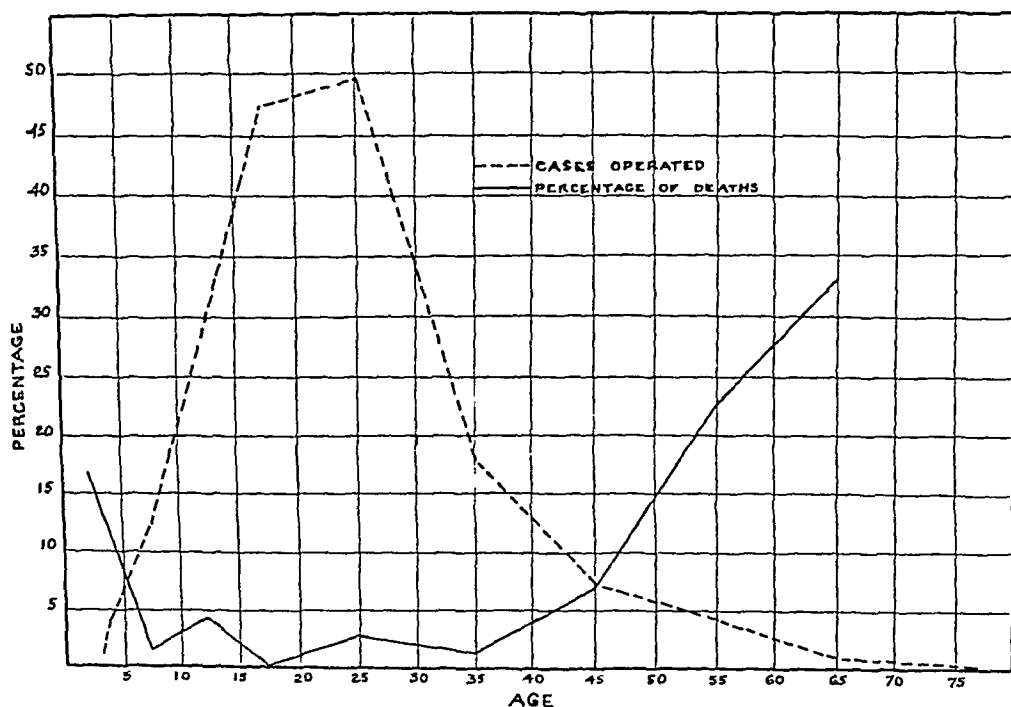


FIG. 3.—Mortality percentage according to age.

return later for appendectomy. The appendiceal stump was inverted with a purse-string suture of linen after the local application of phenol and alcohol. When the cæcum was œdematous and friable this was not attempted; instead, the stump was transfixed and tied with chromic catgut. Fecal fistulæ occurred in only three cases.

An enterostomy was performed once. Quain and Waldschmidt report a primary enterostomy in thirty-one cases and a secondary enterostomy in thirty-eight cases in a series of 1000.

A right rectus incision was employed 519 times, a McBurney incision fifty-nine times, a Battle incision 111 times, and a mid-line incision nine times. At the present time McBurney's is being most favored as it reduces appreciably the patient's hospital stay, and, if exposure is inadequate, it can always be enlarged either upward through the oblique muscles or downward into the rectus sheath.

Ether and ethylene anæsthesia was used in nearly all of the cases. Local anæsthesia was used in some that were too ill to stand ether inhalation, especially when there were pulmonary complications present. At the present time we use spinal anæsthesia in practically all of our adult cases.

Appendectomy was performed without drainage 482 times and with drainage 204 times. Seven abscesses were drained without the removal of the appendix.

Of the twenty-four deaths, nineteen occurred in males. It is possible that men wait longer than women do before they seek medical treatment. During the second and third decades is found the greatest case incidence, but the lowest mortality percentage. Over 70 per cent. of the deaths occurred before the age of fifteen or after the age of forty. These two periods include only 30 per cent. of all the cases. Children under twelve years of age stand operation better than adults over forty. The mortality rate among the former was 6.3 per cent. while in the latter, or older group, it was 16.0 per cent.

The following post-operative complications were recorded on the charts:

|                          |    |                                   |   |
|--------------------------|----|-----------------------------------|---|
| Post-operative pneumonia | 16 | Pyelonephritis                    | 1 |
| Subdiaphragmatic abscess | 4  | Massive collapse of lung          | 1 |
| Fecal fistula            | 3  | Severe cystitis (catheterization) | 1 |
| Evisceration             | 2  | Toxic urticaria                   | 1 |
| Spontaneous abortion     | 2  | Measles—post-operative—three days | 1 |

The average stay in the hospital was 21.4 days, the longest time being 152 days. In children, Beekman found the average stay to be twenty-two days for 145 cases.

Autopsies were done on eighteen out of the twenty-four cases that died. The most common cause of death was peritonitis often complicated by ileus, pneumonia or both. The patient that died in the interval group was very obese, and because of a long exploratory procedure, developed an acute ileus which caused his death. One case was in a tabetic in whom no adequate organic basis could be found to account for his demise. The appendix showed suppuration microscopically.

*Causes of death.*—Peritonitis, 8; pneumonia, 3; peritonitis and pneumonia, 3; peritonitis and ileus, 4; peritonitis, ileus, and pneumonia, 3; ileus and bronchopneumonia, 1; peritonitis and subdiaphragmatic abscess, 1; no reason except *tabes dorsalis*, 1.

#### SUMMARY

1. Sex incidence is equal when all cases are considered, but when the acute cases are separated we find 70 per cent. are in males, while in the chronic cases, the exact reverse is true, with 70 per cent. occurring in females.
2. The peak age incidence is during the second and third decades.
3. The seasonal incidence was highest in summer in this series.
4. A history of recent or coincident infection elsewhere in the body was present in 5.8 per cent. of the cases.
5. There were 339 interval cases with a mortality of 0.3 per cent., 72

## SEVEN HUNDRED APPENDECTOMIES

acute suppurative cases with a mortality of 1.4 per cent., 156 cases with localized peritonitis with a mortality of 2.5 per cent., 112 cases with abscess formation with a mortality of 9.7 per cent., and 21 cases with diffuse peritonitis with a mortality of 38.0 per cent.

6. The type of the disease is in a large part dependent upon the length of time between the onset of the symptoms and the time of operation.

7. In a large proportion of cases it is possible to correlate the clinical picture with the surgical findings. In a small proportion, however, the clinical picture may be very misleading, and it is in this group particularly that there lies great danger of procrastination when immediate operation should be done.

8. Clinical findings are less reliable in determining the prognosis of a case than they are in indicating the probable surgical condition present.

9. A high leucocyte count accompanied by a high polymorphonuclear count usually means good body resistance to a severe infection. This, however, does not prove true in all cases. A leucopenia usually means a poor prognosis.

10. Temperature and pulse are usually but slightly elevated. In children and in the cases with diffuse peritonitis both tend to be higher than in the remainder of the cases.

11. Twenty-eight cases showed pus- red blood-cells or both in the urine.

12. The mortality rate for the entire series was 3.4 per cent. Mortality is highest in the male sex (nineteen out of the twenty-four cases) and highest in children and in the aged.

13. Although an increasing mortality rate according to vital statistics is reported, the operative mortality or fatality rate for appendicitis has decreased. Dividing the 75,858 cases collected into three periods, the average reported operative death rate for the years 1902 to 1910 was found to be 7.6 per cent., decreasing to 5.7 per cent. for the years 1910 to 1920 and to 3.5 per cent. for the years 1920 to 1929.

14. Early diagnosis followed by immediate appendectomy offers the best hope for the reduction of the mortality rate in acute appendicitis.



## ACQUIRED MEGACOLON

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THIS case, due to stricture in the descending and sigmoid colon, is reported because the enlargement of the colon developed while the patient was under our observation; and also, because he has a duodenal diverticulum. Röntgen-ray examinations made soon after the symptoms of partial obstruction developed, and direct examination at the time of operation revealed a normal colon above the sigmoid and descending portions. At the present time röntgenograms show a typical megacolon.

*Literature.*—In most discussions of megacolon the cases are divided into two groups—the congenital type (true Hirschsprung's disease) and the acquired type. The latter includes all those cases which develop after birth. They are due to a partial obstruction which may be intermittent.

Magoun<sup>1</sup> adds an intermediate group which includes those cases developing the typical picture, clinically and in röntgen-ray findings, of megacolon some time after birth without any demonstrable obstruction. A brief review of the literature revealed no case reports in which röntgenograms had been made previous to the development of the megacolon.

Mummery<sup>2</sup> collected 100 cases of megacolon. Fifteen of these had some associated congenital anomaly. Twenty-three had either a partial or an intermittent obstruction. The age incidence was greatest in infancy and after the age of ten years decreased gradually to age seventy. He stated that the age incidence table disproved megacolon is of two types and concluded that the older patients were merely congenital cases in which the patients had survived.

Bailey<sup>3</sup> reported a case of dilatation of the colon in an infant with an imperforate anus. He considered the cause partly congenital and partly mechanical. The possibility of a wholly congenital origin cannot be disproved. The same conclusion would hold for the six cases of simple congenital anorectal stricture with megacolon in early infancy reported by Bremernan.<sup>4</sup>

However, Vernon David,<sup>5</sup> who reported three similar cases, favored the conclusion that at least a part of the megacolons found in infancy were developmental rather than congenital. One of his cases came to autopsy one month after an operation which had relieved the stricture. Only a hypertrophic and somewhat larger than normal sigmoid was found. Before operation röntgenograms had shown the sigmoid filling nearly the entire abdomen. The other two cases became normal clinically after relief of the stricture, but no röntgenograms which had been made after operation were mentioned.

This suggests an explanation for those cases mentioned by Gant<sup>6</sup> in which a megacolon of the sigmoid portion had been excised and then later developed a megacolon of the remaining portions of the colon. Possibly these patients had an unrecognized partial rectal diaphragm or stricture or some other partial obstruction.

Mummery<sup>7</sup> reported a case in which the patient, a man fifty-four years of age, was normal for the first thirty-seven years of his life. Then following an attack of dysentery he developed a severe constipation, followed by the typical symptoms of megacolon. Röntgenograms showed a sigmoid which filled almost the entire abdomen

## ACQUIRED MEGACOLON

with the dilatation extending down to the anus. Just within the anus was an adenocarcinoma which Mummery attributed to the chronic irritation from the great amount of faecal material which accumulated over periods of weeks.

Lefèvre and Jonchères<sup>8</sup> and Rankin<sup>9</sup> reported cases secondary to cancer of the sigmoid. Macaige and Fleury<sup>10</sup> reported a case due to pressure on the rectum by a tumor outside of the rectal wall. In these cases the megacolon may have been present before the so-called cause. Vernon David<sup>5</sup> mentioned a case reported by Treves in which the pelvic rectum was tubular and the size of an adult index finger.

**CASE REPORT.**—T. S., a negro laborer, aged sixty-one, entered St. Luke's Hospital, July 19, 1923, complaining of vomiting and loss of weight. Beginning six weeks before admission, he had been ill for two weeks with pneumonia. One week later he developed gaseous eructations, with which he had nausea and vomiting. This occurred immediately after, or three to four hours after meals.

His abdomen had been distended and considerable flatus expelled. During this six weeks he lost fifty pounds in weight and suffered a marked loss of appetite. Bowel movement occurred by catharsis only. Mucus and blood were noticed in the stool although no blood was seen in the vomitus. There had been some pain about the umbilicus and left flank. At the time of admission the amount of distention and vomiting was decreased.

He had had dysentery for six months in 1918, and rheumatism in practically all his joints at the same time. He was called a typhoid carrier in 1893. A chancre was contracted in 1888 and gonorrhœa in 1883. In 1903 he was told his urine contained sugar. For many years he had had frequent colds and attacks of bronchitis, but never any hæmoptysis or night sweats.

He was a well-developed, somewhat emaciated man who appeared acutely ill. The pupils showed definite reflex rigidity. The abdomen was symmetrical with moderate tenderness to pressure in the right upper quadrant. There were no palpable masses, demonstrable fluid or hernias. Very little distention was present. The knee-jerks could not be elicited.

Rectal examination revealed no palpable pathology. Proctoscopic examination was negative to the height of 6 inches but for a moderate amount of bloody mucus on the rectal mucosa. No amœba were found in this mucus.

The blood count and urinalysis were normal. Blood and cerebrospinal fluid Wassermann reactions were negative. The phenolphthalein output of the kidneys was normal. A two plus reaction was obtained on the two occasions when the stool was examined with guaiac for blood.

**Röntgen-ray Examination.**—A barium injection of the colon was done July 23.



FIG. 1.—The abdomen between attacks of distention.

1923, and reported as follows: (1) Fluoroscopic examination and films taken at the time of the injection reveal an incompetency of the ileocaecal valve. The right portion of the colon is moderately dilated. The descending colon and first portion of the sigmoid are narrow. This finding is constant in all exposures.

(2) Films fifteen minutes after injection are the same as noted above.

(3) Films twenty-four hours after injection show traces of barium as far back as the caecum with retention in the appendix. The descending colon still appears narrow.

(4) In films made forty-eight hours after the injection there is retention in the appendix, and stasis in the colon with narrowing of the descending colon.

July 29, 1923, he was transferred to the surgical service with a diagnosis of tubular stricture of the descending and sigmoid colon probably caused by the six months' attack of dysentery in 1918 with subsequent scar formation and contraction. Operation was done by Dr. H. H. M. Lyle on July 31, 1923. Through a left rectus incision the abdomen was explored. Bands across the descending and sigmoid colon were ligated and cut.

The caecum was ballooned up and well over toward the mid-line. The ascending

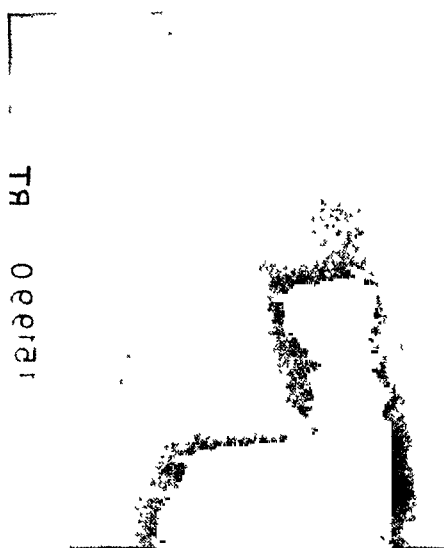


FIG. 2.—Ten-minute gastric rontgenogram. Note the duodenal diverticulum showing between the pylorus and duodenum.



FIG. 3.—Rontgenogram twenty-four hours after barium meal. The lower end of the stricture in the sigmoid shows below the barium retained in the colon.

colon was normal. The transverse colon at about the midportion was collapsed. The splenic flexure could be made out and was normal.

Just below the splenic flexure the colon became cord-like, about 1.5 centimeter in diameter and was adherent throughout its entire length to the parietal peritonæum posteriorly. The sigmoid and upper rectum were a continuation of this condition. Extending over the involved area were several bands of inflammatory tissue crossing the colon at various angles. They appeared to be of old origin. There was no way to identify the sigmoid or rectum because the cord-like structure was continuous throughout. Gas could be forced through the stricture. No area was found suitable for anastomosis distal to the stricture. The abdominal wound was closed.

*Post-operative Rontgen-ray Examination.*—A barium enema was given August 22, 1923, twenty-two days post-operative.

(1) Fluoroscopic examination and films taken at the time of the injection show moderate dilatation of the right portion of the colon. The narrowed portion begins just below the splenic flexure and extends down as far as the junction of the sigmoid colon and rectum. It has the somewhat irregular appearance which was described

before the operation. The rectum is definitely not contracted as seen when the barium first enters that structure.

(2) Films made thirty minutes after elimination reveal no change except that some of the injection has been eliminated.

(3) In films made twenty-four hours after the injection, traces of the injection are seen as far back as the cæcum. The major portion of the injection has been eliminated. This is a marked improvement over the retention shown in the pre-operative films.

*Follow-up Record.*—The post-operative course was uneventful and patient was discharged improved August 24, 1923. He had not been distended or constipated and appeared to be clinically cured up to the time of his discharge.

His history for the next seven years was that of constipation which required constant care. It was so controlled by diet, catharsis and frequent enemas that the patient was able to work regularly. His weight and general condition remained about the same. During this time his prostate enlarged gradually to the size of a small orange with the typical symptoms of partial urethral obstruction.

August 5, 1930, because of the continued troublesome constipation and frequent attacks of abdominal distention, gastro-intestinal rontgenograms were made. These showed the stomach to be normal. A definite duodenal diverticulum filled and contained barium still in the six-hour films. The large bowel appeared to be enormously distended and a long stricture showed in the lower sigmoid.

August 13, 1930, the colon was examined by clyisma and showed a marked distention which appeared to include its three parts. The transverse and ascending colon were enormously distended with gas—definitely, the picture of a megacolon.

He was admitted to St. Luke's Hospital immediately after the clyisma because of nausea, vomiting and abdominal pain. The night before he had been given a large dose of castor oil and before the clyisma a soapsuds enema, but had had no return from either.

His physical examination was very little changed from that of his first admission. He was somewhat more emaciated. His abdomen was enormously distended and so tense that no impression could be made on it with the examining hand. The prostate was so large that examination of the rectum with the finger or a proctoscope was impossible.

Two enemas were entirely unsuccessful. Preparations were made for doing a cæcostomy as first stage to making a short circuit around the stricture. Just before the patient was to have been taken to the operating room, he was able to expell a large quantity of gas and barium. The operation was postponed and by the next morning he was completely relieved. Because of his age and past history, he was sent home and has returned to work.

*Summary.*—When first seen this patient had an inflammatory stricture of the descending and sigmoid colon. Rontgen-ray and direct examination showed a normal colon proximal to the stricture. The cæcum was moderately distended.

After seven years of constipation and mild attacks of obstruction relieved by cathartics and enemas, he now has a definite and large megacolon as shown in the rontgenogram. These pictures also show a duodenal diverticulum.



FIG 4—Barium enema filling only the distal loop of the large megacolon. The remaining loops are distended with gas. Patient's condition did not permit a larger enema.

NOTE.—The first two Röntgen-ray reports are given in detail as the films were all destroyed following the Cleveland Clinic fire. Only colon films were made at the time of the original admission; consequently the duodenal diverticulum was not discovered then. This entire report is quite long for two reasons—first, it covers a period of seven years and two admissions to the hospital; second, because it is unique and was thought to be of sufficient importance to require considerable detail.

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# IS TOXÆMIA THE CAUSE OF DEATH IN UNCOMPLICATED INTESTINAL OBSTRUCTION?

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THESE experiments are not presented as proof of a thesis but are offered as evidence in support of the point of view that toxæmia is relatively unimportant in causing death from simple intestinal obstruction. The bulk of the work on this subject has been directed by the opposite opinion and many ingenious experimenters have sought to demonstrate the toxin and its mode of action, yet it has never been isolated and its nature has remained clothed in mystery and a subject of conjecture. From time to time there have been dissenting voices<sup>2, 3, 9, 10</sup> which stated that other factors, such as loss of food, fluids and normal secretions, might be responsible for the fatal result, but the general cry of "find the toxin" still prevails. That these substances are lost is not doubted, for even without vomiting their accumulation in a distended bowel renders them just as useless to the organisms as would their elimination. So it would appear that their loss may have influence and serve to confuse the issue by adding a multiplicity of factors to the lethal effect. By their conservation the influence of the toxin alone may be judged. This would necessitate retention of gastric and duodenal secretion (including bile and pancreatic juice) and administration of food and fluid. An experiment was planned to shunt all of these substances below the point of obstruction but for technical reasons only a part of the gastric secretion could be retained. This gives opportunity for the evaluation of the effect of the toxin alone without the complication of other factors. Surprisingly enough, if the upper-tract secretion combined with food and fluid is retained by its absorption below the point of obstruction, then no true toxæmia develops.

*Method.*—Adult dogs are used as experimental animals. The three-stage operative procedure is shown in Fig. 1. The first stage consists of mobilization of the duodenum at Treitz ligament, transection of the stomach, closure of the distal end and anastomosis of the proximal end to the upper jejunum. The second stage is done by cutting the end of the duodenum free from the gastric anastomosis, turning in the blind ends and anastomosing the duodenal segment into the jejunum at a point about 50 centimetres below the gastrojejunal anastomosis. At the third stage, a gastrostomy is done in the blind distal gastric segment and the jejunum is obstructed above the anastomosis with the duodenum. An attempt to shorten the operative procedure by combining the first and second stage was made, but this resulted in the death of five out of seven animals and was abandoned. It is possible to omit stage two by bringing down the duodenal segment and, after obstructing the jejunum, implanting it into the distal jejunal loop with an end-to-end anastomosis.

After the final operation for obstruction the animals are fed a liquid diet, consisting largely of milk, through the gastrostomy opening, and water is also supplied by this route. Since a portion of the stomach is in the obstructed loop, then some gastric secre-

tion is lost by vomiting and hence the chlorides may be depleted after an interval of about two weeks. If this occurs, one or two grams of NaCl are added daily to the diet until the normal balance is reestablished. (See Fig. 2.) The animals are allowed food and water by mouth *ad lib.* Blood for chemical estimation of the non-protein



FIG. 1.—The operative procedure, done in three stages, is designed to divert the bile, pancreatic juice, duodenal and a part of the gastric secretion to a point below the intestinal obstruction. Food and fluid are supplied through the gastrostomy.

nitrogen chlorides and carbon-dioxide combining power is taken before and at frequent intervals after the obstruction. The contents of the obstructed loop are examined bacteriologically, especially for *B. welchii*.

*Results.*—In all, fifteen dogs were operated upon, of which seven died from various causes before obstruction. After the final operation for obstruction, one dog died in twenty-four hours and another animal died in twelve days from a poorly functioning

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duodenal anastomosis, leaving six obstructed dogs for study. These animals either died or were sacrificed at the end of a month. None of them developed the toxæmia of intestinal obstruction as we ordinarily conceive of the term. They vomited from time to time a very foul vomitus containing *B. welchii* and other organisms but they did not develop the rapid onset of lethargy, weakness, stupor or blood-chemistry changes (see Fig. 2) that are associated with intestinal obstruction, nor did they die at the usual time. On the contrary, they are alert and active and appear to be in good health for at least two weeks after the obstruction. At the end of this time they gradually

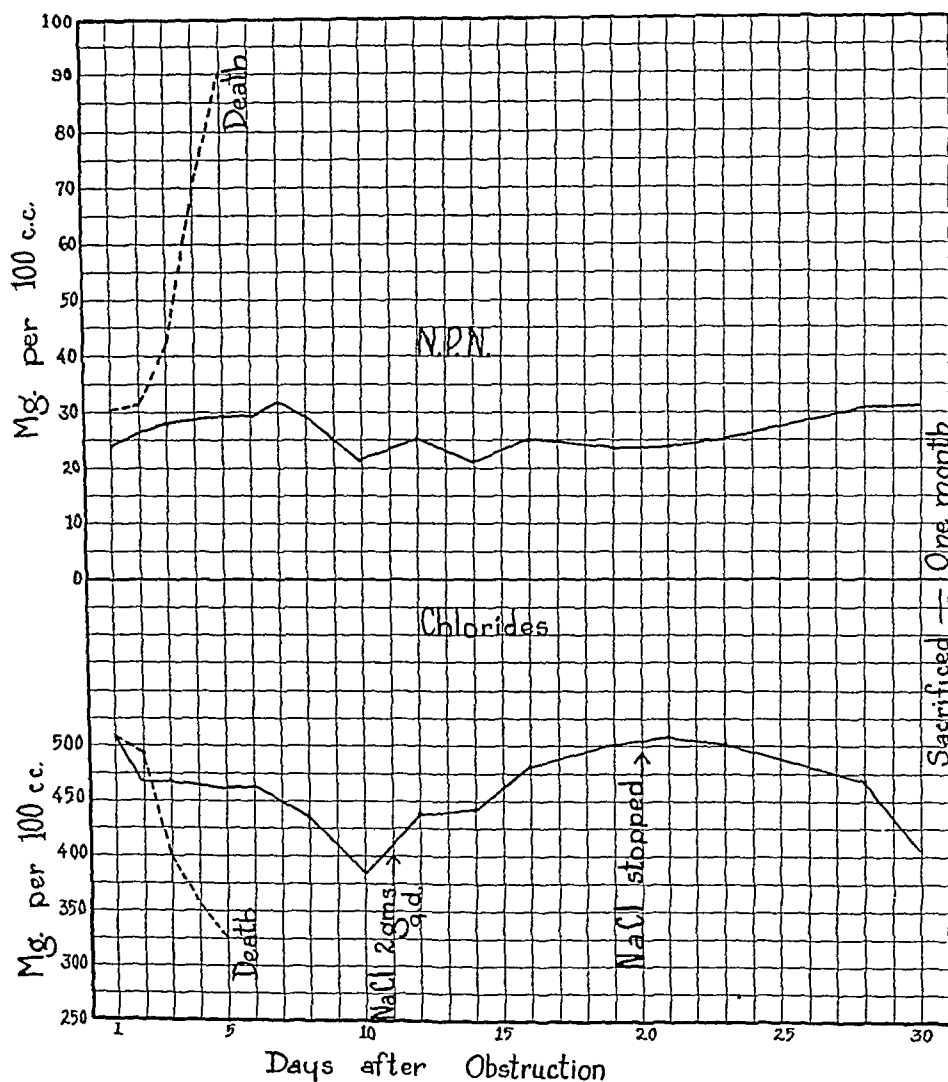


FIG. 2.—A comparison of the blood-chemistry changes in simple, experimental, intestinal obstruction: (a) with conservation of upper-tract secretion, food and fluid (solid line), and (b) in the usual experiment with the loss of these substances (broken line) in which the N. P. N. rises, the chlorides fall and early death occurs. Both dogs have a high obstruction at a point 40 centimetres from the stomach. The influence of the addition of NaCl to the diet is shown.

begin to lose weight and as this progresses there may be associated loss of strength so that a state of inanition or chronic nutritional disorder develops. This condition becomes very pronounced at the end of a month and the animals often develop an intercurrent infection, an intractible diarrhœa or a chronic sore from pressure of the dressings and may die. Habler<sup>4</sup> has shown that a somewhat similar operative procedure but without the intestinal obstruction causes this same metabolic disturbance.

*Discussion.*—Since the animals survived for a month, it seemed evident verification of the criteria of the experiment. They were sacrificed at the expiration of that period. At that time they were usually sick and always



cachectic and in a state of inanition, but this condition was quite different from the syndrome associated with the acute "toxæmia" of intestinal obstruction. The cause of this state of inanition is an interesting problem in itself but is without the province of this study. It may be associated with a derangement of absorption of the upper-tract secretions which are diverted to an abnormally low point in the small intestine.

The fact that when starvation, dehydration and loss of normal secretion are eliminated from simple intestinal obstruction, no toxæmia results is interpreted to mean that no specific toxæmia exists. There are other proponents of this opinion and additional evidence may be presented for its support. Habler<sup>4</sup> and Jenkins<sup>6</sup> have performed experiments somewhat similar in principle with the same result but have held the interpretation that the duodenal contents are necessary for the formation of a toxin in intestinal obstruction. Jenkins mentions the alternative that these secretions may be necessary for the preservation of life. Dragstedt and Ellis<sup>1</sup> have shown that the loss of gastric secretion is fatal in a few days. That the loss of upper intestinal juices is harmful has been stated by Wilkie<sup>10</sup> and may be inferred from the results of Haden and Orr<sup>5</sup> who found that obstructed dogs having a simultaneous jejunostomy live a much shorter time than do those with only obstruction. There is experimental<sup>7</sup> and clinical evidence to show that if the contents of the obstructed loop are allowed to remain after the obstruction is relieved recovery may be more rapid than with its removal. Perhaps the most convincing evidence is from the experiments of White and Fender<sup>9</sup> who collected the vomitus from obstructed dogs and reinserted it through an enterostomy below the obstruction. This procedure would give the greatest chance for absorption of a toxin if it were present, but not only did the animals live but also they showed no evidence of toxæmia.

A consideration of these data permits of the interpretation that in simple, uncomplicated, intestinal obstruction, there is no need for the theory of death from a specific toxin for the loss of upper-tract secretion combined with anhydræmia and starvation is sufficient to cause the lethal effect. Conversely, with the conservation of food, fluids and normal secretion no specific toxic effect is noted from the intestinal obstruction.

It must be borne in mind that the addition of tissue damage, strangulation and peritonitis to this result materially complicates the picture and these must be studied as individual factors. It is possible that they produce their effect by creating a portal of entry to the blood-stream for the deleterious products normally present<sup>8</sup> in intestinal contents and not by the formation of a specific toxic substance.

It follows that if the data are interpreted to mean that there is no specific toxin resulting from simple intestinal obstruction, then therapeutic efforts should be directed toward the relief of anhydræmia and starvation, but, much more important, to the preservation and restitution of the substances lost in the gastric and duodenal contents. The demonstration by Haden and Orr<sup>5</sup> of the beneficial effect of the administration of fluids and of the chlorides lost from the gastric juice is one of the important contributions to the treat-

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ment of this condition. The effect of restitution of the substances lost from the duodenal secretion, bile and pancreatic juice is an unexplored field. Early operative intervention is indicated to relieve obstruction and to prevent tissue damage from excessive distension, strangulation or peritonitis but for those procedures designed to drain off the "toxic" contents of the obstructed loop will be substituted measures to conserve these secretions. Thus it is seen that the adoption of the point of view that toxæmia is relatively unimportant in causing death from simple, intestinal obstruction suggests stimulating possibilities of new methods of treatment.

### CONCLUSIONS

1. Studies on the toxæmia of simple intestinal obstruction are complicated by the factors of loss of upper-tract secretion, anhydræmia and starvation.

2. The shunting of food, fluid, and the secretions in the stomach and duodenum to a point below the obstruction results in the absence of manifestations of toxæmia.

3. This is interpreted as evidence in favor of the point of view that no specific toxin is produced by simple intestinal obstruction.

4. The complications of tissue damage, strangulation and peritoneal contamination add other factors to the effect of the original obstruction and must be analyzed separately.

5. From the practical standpoint of the care of patients with intestinal obstruction it is safer to assume that they all have potential or actual tissue damage from distention or strangulation and to institute early operative intervention for its relief.

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## THE SURGICAL ASPECTS OF ASCARIASIS

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IN CONSIDERING diseases requiring surgical intervention ascariasis is rarely thought of, for while harmless in most instances, it may, at times, produce the most imposing pathological states. Because of its comparative rarity in this part of the country cognizance of its ability to produce major surgical conditions is frequently overlooked. The examination of stools for the detection of these parasites will become more frequent, if we bear in mind clearly the serious disturbances which may arise as a result of their presence.

It is indeed important to understand the cycle of development in man, since the worm in both its larval and adult stages is actively migratory. Briefly, the course of development is as follows:

The eggs pass out the intestines of an infested animal (pig or man) in the fæces. The eggs, however, are not infective until the contained embryos develop to a vermiform stage, which requires a period of two weeks or more, according to the temperature of the surrounding medium, oxygen supply and moisture. Accidentally the embryos may hatch outside the body, but in this case they perish quickly. Within the highly impermeable egg-shell, the fully developed embryo is very resistant to cold, dryness and other unfavorable conditions and may remain alive for long periods of time—five years or possibly longer. If swallowed by some mammal, the eggs that contain fully developed embryos hatch in the small intestines. They will also hatch if artificially introduced beneath the skin.

Unless accidentally carried out of the body in the fæces, the newly hatched larvæ penetrate the wall of the small intestines and pass into the blood-stream to the liver, though some possibly go more directly to the heart; in both cases apparently aided by the circulation. From the liver, where they remain in most cases only a few days, they migrate to the lungs, evidently by the hepatic veins, inferior vena cava, heart and pulmonary arteries. They are stopped in the lungs by the capillaries, enter the air vesicles and bronchioles, pass up the bronchi and trachea, then pass into the œsophagus and finally reach the small intestine, where, if the animal infested is a suitable host, they establish themselves and continue their development to maturity.

*Ascaris lumbricoides* is famous for its habits of wandering about and making its appearance in strange places, and it is not surprising that disturbances resulting from the presence of the parasites in organs other than the intestines should frequently occur.

Recently one of us (E. I. G.) was called to operate on an acute surgical

abdomen. The diagnosis was not definite and was to be in the form of an exploratory laparotomy.

N. C., aged seven, was admitted to the hospital September 1, 1929, with the following history: On the preceding day the boy, who previously had been in perfect health, attended a party. He returned home that evening complaining of severe abdominal pain. On being questioned by his mother, the child stated that he had been kicked in the abdomen by one of his playmates while at the party. The boy was put to bed but all night complained of recurrent attacks of excruciating pain lasting from fifteen to thirty minutes. The following day the boy was admitted to the hospital.

His temperature was  $101.2^{\circ}$ , pulse 130, respiration 24. His white count was 12,000 and the differential count was reported to contain 78 per cent. polymorphonuclear leucocytes, 20 per cent. large lymphocytes and 2 per cent. small lymphocytes. The urine was negative. The red blood count read 4,370,000.

The abdomen was rigid with definite tenderness in the right lower quadrant. Rectally the patient had tenderness over the right side. A diagnosis of a ruptured viscus was made by the interne.

When the boy was seen by a surgical colleague the attack had subsided, the patient was comfortable and he could not substantiate the diagnosis of an intra-abdominal lesion.

The patient continued to have recurrent attacks of severe abdominal pain coming on at hourly intervals. The abdomen would become rigid, the boy would roll about in bed, hands clasped to abdomen, and become markedly cyanotic. After fifteen or twenty minutes the paroxysm would abate, the abdomen would become flaccid and the boy would apparently be normal, only to have a recurrence within an hour. The pædiatric department felt that it was advisable to explore the abdomen.

Although the diagnosis was not clear, yet with a history of recurrent abdominal crises following an injury to the abdomen, it was thought justifiable to explore the abdominal cavity. Before taking the boy to the operating room another differential count was made which revealed a 40 per cent. eosinophilia. Immediately a parasitic infection suggested itself and an examination of the stool, following a small enema, revealed many ova of *ascaris lumbricoides*. A diagnosis of incomplete intestinal obstruction due to round worms was made and treatment was instituted immediately. Within two days the boy passed a mass about the size of a walnut composed of some three hundred worms tightly packed together, and many free worms were found floating on top of the saline solution. The child's complete recovery then followed.

In reviewing the literature of ascariasis one immediately realizes that any of the abdominal organs may become the seat of a severe and often fatal disease.

*Intestinal Obstruction.*—Intestinal obstruction is probably the most common surgical condition resulting from the presence of the round worms in the intestinal tract. Two definite types of intestinal obstruction are recognized: an obturating type—as a result of the massed collection of worms, as was present in this case; and a spastic type which may be caused by only one or several worms.

The worms have a tendency to collect in masses and as they pass through the small bowel are hindered in their progress by the narrow lumen, resulting in an occlusion of the bowel. Just why the ascarides tend to congregate in masses has not been definitely established. Schlössmann is of the opinion that the clumping of the worms is due to their own movements and not to the action of peristaltic waves. In some portion of the bowel an *ascaris*

curls up. Others in the neighborhood trying to get into the smallest place possible work their way into the curled worm, soon forming a knot. The presence of such a collection of worms acts as a foreign body causing a spasm of the bowel.

*Ascaris lumbricoides* is famous for its singular tendency to get into tight places. Stiles has collected a number of interesting cases in which the worms were found threaded through the eye of a shoe button which had been swallowed. He cites another case in which a child had swallowed several dress hook eyes. When the eyes were finally passed each was threaded by a worm.

Rost, however, is of the opinion that a chemical secretion is given off by the worm which causes a spasm of the bowel. He found that an extract of the digestive and genital organs increase the tonus of the intestine of the cat, and concluded that spasm was due to the death and disintegration of the worm. Jaroschka, disagrees with this theory, and is supported by Sohn and Kuester, believing that the obstruction is mechanical.

Glass and Bloom report a case of acute intestinal obstruction in a boy of nine in which the duodenum and whole jejunum were tightly packed with masses of ascarides. Ludlow reports a case of acute intestinal obstruction in a boy of sixteen in which 30 centimetres of gangrenous bowel were found, but only five worms were present. Ludlow was of the impression that in his case obstruction was caused by the irritant action of the ascaris rather than by a mechanical occlusion. In the case reported by Alles, the worms were so tightly packed that upon opening the abdomen the bowel looked like a sausage, being about the size of the surgeon's arm.

Cases of intestinal obstruction due to *ascaris lumbricoides* have also been reported by Zoloff, Takaka, McGlannan, Perret and Simon, Levy, Watkins and Moss, Heiser, Holland, Baugh, Levin and Porter, Jaroschka, and Manhorya.

*Perforation of the Bowel* due to *ascaris* is not uncommon and the literature contains many such case reports. Ludlow reports a case of generalized peritonitis, the abdominal cavity being bathed in about one thousand cubic centimetres of milk-like pus. Three worms were found in the abdominal cavity. There was a hole in the ileum, one foot from the cæcum and through this hole another worm protruded.

Gilberti reports two cases of perforation of the intestines by *ascaris*. In both cases there were perforations present with worms free in the abdominal cavity. Schlössmann reports six cases of peritonitis in which the worms had perforated the bowel wall to lie free in the abdominal cavity. Frequently, cases of perforation and peritonitis due to *ascaris lumbricoides*, in which the worms are found in the abdominal cavity, yet in which no perforation can be demonstrated in the bowel wall, have been reported. The prevailing opinion is that the opening closes immediately after the passage of the worm. Whether an adult worm can go through a normal wall is questionable. Most authorities feel that some destructive process must first be present before the *ascaris* can perforate the bowel. Fleury and TaKeuchi have shown that there is local hyperæmia, œdema and necrosis present before perforation can occur. That some injury to the intestinal wall must take place before perforation ensues is beautifully illustrated by the report of Jaroschka in which during an operation for intestinal obstruction caused by round worms, the serosa of the small bowel at the junction of the jejunum and the ileum was torn, the muscularis and mucosa remaining intact. The serosa was then repaired and the abdomen closed. Two days after the operation the patient presented signs of diffuse peritonitis. It was thought that perhaps the suture line broke leading to a perforation. At the autopsy it was found that at the border of the jejunum and ileum where the tear had occurred two worms were found penetrating the wall, one extending 4 centimetres

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through the wall, the other 10 centimetres. One worm was found under one of the sutures. The original suture line was intact. Jaroschka concludes that in handling cases of intestinal parasites, when it is necessary to open the bowel, in case of a tear, all layers and not only the serosa should be repaired. He also feels that if perforation is present during life the mucosa and muscularis must be damaged.

Gilberti concludes that the ascaris fastens itself to the bowel wall, setting up an irritation which leads to ulceration, necrosis and perforation. He admits that the mouth of the ascaris is able to injure the bowel wall directly, enough to entail perforation in time. Gerlach also makes mention of a case of ascaris ileus with peritonitis in which there were numerous areas spread throughout the bowel of definite disturbance in the mucosa, muscularis and submucosa, eventually leading to a perforation.

Wyss found the intestinal serosa turbid and dark red. One ascaris was found free in the abdominal cavity. Two more were coming through the hæmorrhagic intestines, and hæmorrhagic areas were found in the mesentery. The intestinal wall was necrotic in many places and very friable. Two perforations were found.

Freudenthal's case is remarkable in that a worm 25 centimetres long was found free in the abdominal cavity, but no evidence of any peritoneal reaction was found. His patient had been ill for six months and was finally operated, the diagnosis being "chronic appendix." At operation the ascaris was found and removed together with the appendix. The question arises as to the mode of entrance of the ascaris into the abdominal cavity. There being no evidence of peritoneal reaction, either healed or recent, rules out a perforation. Did the 25-centimetre worm grow from its larva in the abdominal cavity? This is an interesting conjecture but Freudenthal feels that it is the only logical conclusion.

*Pancreatic Disease Due to Ascariasis.*—Because of the ability of the worms to wander about, the pancreas has frequently been the seat of pathology. Rigby reports a case of acute pancreatitis in a woman of thirty caused by ascarides. At autopsy there was considerable fat necrosis throughout the peritonæum, including the under surface of the diaphragm. On opening the duodenum, an ascaris was found projecting from the ampulla of Vater into the lumen of the gut. The pancreatic duct was opened and the body of the ascaris found passing along the duct, then turning into the duct of Santorini, so that both ducts were blocked effectually.

Gallie and Brown report a case of acute hæmorrhagic pancreatitis caused by round worms, occurring in a child two and a half years old. The history was typical and at operation a blood-stained fluid with fat necrosis was found. The pancreas was large, swollen and covered by a mass of acutely inflamed omentum. Fifteen hours after operation the child vomited a full-sized round worm following which the convalescence was uneventful. The authors were of the opinion that the symptoms were the result of the round worm which had introduced its head into the ampulla of Vater, allowing a back flow of bile or intestinal juices into the pancreas, or had created such an irritation in the duodenum that the ampulla became closed by the resulting inflammatory reaction.

Novis reports a remarkable case of partial obstruction of the pancreatic duct by a round worm with recovery after surgical intervention. After recurrent attacks for eight days operation revealed an enlarged pancreas which was split open from head to tail. The pancreatic duct was incised and a full-sized living worm and a partially disintegrated worm extracted. The patient made an uneventful recovery.

Eberle's case presented two worms in the pancreatic duct together with great numbers of worms in the common duct, hepatic duct and parenchyma of the liver.

Altman reports the autopsy findings of his case in which the pancreas was markedly increased in size and many worms were found in the duct of Wirsung. Clumps of worms were also found in the tail of the pancreas.

Pfanner also reports a case of acute pancreatitis caused by *Ascaris lumbricoides*.

*Ascaris in the Bile Ducts, Gall-bladder and Liver.*—The liver, bile passages and gall-bladder have not been immune to the ravages of the round worm. One of us (J.M.G.) witnessed an autopsy performed by Chiari in Vienna on a patient dying of a severe jaundice. The common duct was found packed with worms.

Worms in the gall-bladder, bile ducts or liver present symptoms indistinguishable from stones or other infective processes. Worms within the gall-bladder have presented symptoms not unlike gall-stones. Worms in the bile ducts present symptoms exactly like those produced by stones. Painless, progressive jaundice suggesting carcinoma of the head of the pancreas has been caused by ascaris.

Borger in 1891 found fifty-nine cases of round worm in the bile ducts. Tsujimura in 1922 collected thirty-three cases. Brayne's case was profoundly jaundiced, and at autopsy the gall-bladder, common duct, cystic duct and hepatic ducts were full of worms. On sectioning the liver numerous large worms were found in the ducts. The cut liver presented an extraordinary appearance. Two or three worms were cut across, but some six or eight were peeping out from the cut end of the bile ducts on each side of the incision.

Shim's case is interesting in that the patient, a male of thirty-eight, had had recurrent attacks of pain in the right upper quadrant for six years. At operation a long calculus was found in the common duct. The centre of the calculus contained the ova and remnants of a round worm.

Eberle's case is that of a young boy of nine, operated on because of pain and severe jaundice. A worm was found in the gall-bladder and three in the hepatic duct, all living, and from 20 to 25 centimetres long. Eleven days later two more worms were removed from the bile ducts. This is the first case on record according to Eberle in which an operation was performed for invasion of the biliary apparatus under the age of ten. His second case was a woman of forty-five. At operation six gall-stones were removed, six living ascarides were removed from the common duct, twenty-five from the hepatic duct, thirty-five from the parenchyma of the liver and two from the pancreas. Both the liver and the pancreas were studded with small abscesses.

Degorce reports a case of violent hepatic colics recurring for seven years. At operation many stones were removed from the common duct. The patient recovered but died six months later of pulmonary tuberculosis. Autopsy showed about forty stones in the biliary passages, all of which contained eggs of the round worm. Sectioning one of the largest stones, a filament one and one-half inches long was found which proved to be a small ascaris.

Cases of increasing painless jaundice simulating malignancy of the head of the pancreas have been reported. Merteus and Panayatation report cases of this type without pain, without temperature, but with progressive increasing jaundice which cleared up spontaneously after expulsion of the round worms.

A number of cases of abscess of the liver have been reported. Kirkland, Dunkel and Leick each report a case of ascaris lumbricoides found within an abscess of the liver. Eberle reports two cases of liver abscess caused by the worms, one a woman of fifty-two and the other a child of seven. The first patient complained of severe pain in the right upper quadrant radiating to the shoulder, septic temperature, nausea, vomiting and jaundice. The liver was palpable. A diagnosis of cholelithiasis was made but at operation a hard mass on the under surface of the left border of the liver was found, which when opened contained pus and worms.

The second case, a girl of seven, complained of severe abdominal pain, pain in the right upper quadrant, septic temperature, but no jaundice. The pre-operative diagnosis

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was liver abscess and septic cholangitis. At operation a large mass was removed from the left lobe of the liver. This mass contained considerable pus and many worms. No connection between the abscess and bile passages could be determined. Hartman-Keppel reports two similar cases.

Multiple liver abscesses, varying in size, caused by round worms have been reported by a number of investigators. Altman's case was a little girl of two, complaining of severe abdominal pain and symptoms pointing to a meningitis. At autopsy a pneumococcus meningitis was found. The stomach, duodenum and ileum were filled with balls of worms. The mucosa of the bowel was extremely friable. One worm was found extending into the papilla of Vater. The hepatic duct was full of worms and throughout the ducts of the liver worms were found, the ducts being widened and containing bile pus. Scattered through the liver were small cholangitic abscesses. The pancreas was large, dark and worms were found in the duct of Wirsung, while in the tail of the pancreas clumps of worms were found. The infection in the liver and pancreas was due to bacteria brought in by the worms, together with the widening of the bile passages and retention of secretions.

*Ascariasis in the Gall-bladder* has been reported nine times. Morton has recently collected cases in which the worm was found within the gall-bladder and undoubtedly the cause of the patient's symptoms. A pre-operative diagnosis is impossible—the outstanding symptom being severe biliary colics. In a case reported by Degorce, necropsy showed many stones present within the gall-bladder, all of which contained the eggs of the round worm. On section of one of the largest stones, a filament one and one-half inches long was found which proved to be a small ascaris.

*Appendicitis* due to *ascaris lumbricoides* is not uncommon, the literature containing many reports of typical attacks which at operation were shown to be caused by the ascaris.

Ludlow reports three cases of perforated appendices with localized collection of worms in the right iliac fossa.

Portly's case had already perforated but was operated before any peritonitis had occurred. The worm was found lying free in the abdominal cavity. Schlössmann reports eleven cases of appendicitis due to *ascaris lumbricoides*.

Perthes reports six cases of *ascaris* in the abdomen associated with appendicitis. The appendices were either perforated or gangrenous and the worms were alive. The author conjectures whether the appendicitis was the result of the *ascaris* or whether both were present at the same time.

*Ascaris in the Fallopian Tube.*—A number of cases of *ascaris lumbricoides* found in the Fallopian tubes have been reported. Nacken reports a case of pyosalpinx in which he found a worm measuring 25 centimetres. The ileum in this case was firmly attached to the tube and a perforation of the ileum leading to the tube was demonstrated.

Adeodato's case presented the picture of a cystic salpingo-oöphoritis. At operation the cystic tube ruptured and an *ascaris* 10 centimetres long dropped out. No demonstrable opening between the cystic mass and the intestines was found in this case.

Maxwell reports a tubo-ovarian abscess in which no communication between the bowel and tube could be demonstrated. He feels that the possibility of the worm's passing through the bowel with subsequent closure of the opening must be entertained. He also feels that there is a possibility that the worm might have gone into the vagina, ascended through the uterus and into the tube.

Hofstotter's case is similar to the preceding one. In his case, however, the patient died of a perforated cæcum due to ascariasis. At autopsy a right pyosalpinx was found and a worm 15 centimetres long was found in the left tube, the fimbriated end of which was closed. This proved that the worm did not enter the tube after death, for otherwise the tube would have remained open. That it was impossible for the worm to enter the tube via the rectum, vagina and uterus was ruled out by a very marked stenosis at the uterine end of the tube which would not permit the passage of the finest probe. Hofstot-



ter believes that after the perforation, the worm wandered over to the left tube, as it was impossible to gain entrance into the right side because of a pyosalpinx.

*Ascaris Lumbricoides in the Urinary Bladder.*—We have been able to find only one case report, in recent literature, in which the worms were found in the urinary bladder. Carsten reports such a case occurring in a man of sixty-nine who consulted him because of a twenty-four-hour urinary retention. A catheter was easily inserted and after twenty-four hours was removed because no urine passed through the tube. On removing the catheter the opening was blocked by a 20-centimetre ascaris. No urinary disturbance occurred after the worm was removed. Three days later, the patient again returned because of retention of urine. On insertion of a catheter another worm measuring 10 centimetres was removed. Following this the patient made an uneventful recovery.

Just how the worms gained entrance into the bladder makes interesting conjectures. Did they perforate the bowel and the urinary bladder? Was there a fistula between the bowel and bladder? Did the worms get into the bladder by way of the kidneys? Did the eggs get into the bladder by way of the lymph-stream?

Examination of the urine sediment showed the presence of many eggs. Examination of the bladder showed no defect in the wall. Examination of the rectum failed to reveal evidence of a recto-vesical fistula. Methylene blue introduced into the bladder failed to make its appearance in the rectum. Carsten feels that the logical conclusion is that the ascaris' eggs entered the urinary bladder by way of the lymph-stream.

*Empyema and Pulmonary Gangrene Due to Ascariasis.*—Middleton reports the autopsy findings in a boy of four in which the left pleural cavity contained 500 cubic centimetres of thick pus. The left lung was practically collapsed, the lower lobe airless, firm and brownish green. Two and a half inches of the cephalic extremity of a round worm which measured 14 centimetres in length protruded into the left pleural cavity through a perforation of the lower lobe posteriorly near the hilum. The tract along which the worm had passed could be traced into the lung substance. The worm had apparently been regurgitated from the stomach to the level of the larynx and aspirated into the left bronchus, which it perforated to reach the lung.

Stiles refers to forty cases in which the adult worms have been found in the lungs, causing gangrene and pneumonia.

Wyss reports two cases of pleural effusion in which the eggs of the ascaris lumbricoides were found. The first case is that of a patient with liver abscesses due to ascariasis with perforation into the pleural cavity. The second case is that of a child one and one-half years old. The pus in this case contained many eggs of ascaris lumbricoides. Here the cause of the empyema was not determined.

The round worm has been found in an inguinal ulcer as reported by J. Wiegiersma.

Kortzeborn did a resection of the stomach which was followed by death due to peritonitis. At autopsy the abdomen contained a number of worms which had escaped through the suture line and produced the peritonitis.

Blanchard compiled eighty-one cases in which the ascarides escaped through the body wall, twenty-nine through the umbilicus, thirty through the groin, ten at unstated points of the abdomen, two by the hypochondrium, two by the lumbar region, two by an inguinal abscess and one each by the sacral, pubic, perineal region, abscess of the thigh, inferior portion of the thorax and linea alba.

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# SPINAL ANÆSTHESIA

AN ANALYSIS OF 497 CASES

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THE following is a report of the experience with the use of spinal anæsthesia at the Mount Sinai Hospital in New York City for the years 1927, 1928 and 1929. No attempt will be made to discuss the relative value or the physiological aspects of spinal anæsthesia, but we will present our observations in a series of cases over a period of three years. It was the impression of the surgeons of the hospital, gained both from the literature and personal communications, that spinal anæsthesia was receiving an enthusiastic reception without an adequate recording of all the observations attendant with its practice. In this series, spinal anæsthesia was used in selected cases. For the most part, these cases were either those in which there were contraindications to a general anæsthetic, or those in which the operative procedure, usually abdominal, was of some magnitude.

*Number of Cases.*—497.

|   |           |
|---|-----------|
| <i>Age Distribution.</i> —10-20 years ..... | 7 cases   |
| 20-30 years .....                           | 46 cases  |
| 30-40 years .....                           | 87 cases  |
| 40-50 years .....                           | 139 cases |
| 50-60 years .....                           | 128 cases |
| 60-70 years .....                           | 82 cases  |
| 70-80 years .....                           | 8 cases   |

*Sex Distribution.*—Male, 327; female, 170.

*Technic.*—In most cases, the individual surgeon acted as his own spinal anæsthetist, the patient being carefully observed throughout the course of the operation by a regular nurse staff anæsthetist.

*Drug Used.*—The drug used was almost exclusively neocaine in crystalline form dissolved in the spinal fluid.

*Dosage of Drug.*—The usual dose of neocaine was 120 milligrams.

*Position of the Patient.*—The lumbar puncture was done with the patient either in the sitting or in the lateral position. Immediately after the injection the patient was placed in slight Trendelenburg position.

*Preliminary Medication.*—Morphine and atropine were administered prior to the procedure in 345 cases, and codeine and atropine in thirteen cases. Ephedrine was given in 145 cases. The usual dose of ephedrine was 50 milligrams.

*Level of Injection.*—The level of injection was specifically noted in only sixty-eight cases. Of these, twenty-seven were administered above the second lumbar vertebra and forty-one below that site.

*Blood-pressure Changes.*—Accurate blood-pressure determinations were recorded in 117 cases. In ninety-nine cases there was a fall in blood-pressure of from 10 to 100 millimetres of mercury. This fall occurred in most cases within fifteen to thirty minutes following the injection of the anæsthetic. Marked drops in blood-pressure (50 millimetres or more) were noted in thirty-five cases. These marked drops in blood-pressure had severe accompanying clinical manifestations in twelve cases, six of whom were over sixty years of age, and nine of whom were over fifty years of age. In all cases in which a fall in blood-pressure was observed, ephedrine had been used prior to induction. In eighteen cases there was a rise in blood-pressure which was maintained above the ante-operative blood-pressure throughout the course of the operation. The rise in most cases was within the first ten minutes. Ephedrine had been used in sixteen of these eighteen cases.

No relation could be determined between the changes in blood-pressure and the level of the injection. Striking falls in blood-pressure were observed as frequently in injections below the second lumbar vertebra as in those injected above that level.

*Adequacy of Anæsthesia.*—The anæsthesia was considered adequate throughout the operation in 326 cases—65.6 per cent. No supplementary anæsthesia was used in this group. In these cases the duration of the operation was as follows:

| No. of Minutes | No. of Cases |
|----------------|--------------|
| 0-10 .....     | 4            |
| 10-20 .....    | 26           |
| 20-30 .....    | 38           |
| 30-40 .....    | 54           |
| 40-50 .....    | 43           |
| 50-60 .....    | 25           |
| 60-70 .....    | 27           |
| 70-80 .....    | 27           |
| 80-90 .....    | 23           |
| 90-100 .....   | 13           |
| 100-110 .....  | 8            |
| 110-120 .....  | 6            |
| 120-130 .....  | 4            |
| 130-140 .....  | 3            |
| 140-150 .....  | 1            |
| 160-170 .....  | 2            |
| 180-190 .....  | 1            |
| 200-210 .....  | 1            |
| 210-220 .....  | 2            |

It should be noted that this is not an absolutely accurate record of the actual length of anæsthesia. In the very short operations, the anæsthesia was usually of longer duration, and in some of the very long cases the anæsthesia had partly worn off toward the end of the operation even though no supplementary anæsthesia had been given.

There were eighteen cases in which the anæsthesia was satisfactory but in which the duration of the operation was not recorded.

## SPINAL ANÆSTHESIA

The anæsthesia was entirely unsatisfactory in eight cases (1.6 per cent.). In three of these it appears that the technic of injection was faulty. In a few cases, the exact number not known, there was noted a lack of relaxation of the abdominal wall, although the patient appeared to suffer no pain.

The spinal anæsthesia had to be supplemented in 163 cases (32.8 per cent.). In sixty-four of these, the exact time at which the supplementary anæsthesia was begun was noted.

| No. of Minutes | No. of Cases |
|----------------|--------------|
| 10-20 .....    | 2            |
| 30-40 .....    | 8            |
| 40-50 .....    | 7            |
| 50-60 .....    | 9            |
| 60-70 .....    | 8            |
| 70-80 .....    | 10           |
| 80-90 .....    | 7            |
| 90-100 .....   | 6            |
| 100-110 .....  | 4            |
| 120-130 .....  | 3            |

*General Condition of the Patient before Operation.*—A large variety of medical complications was found in the group of patients under consideration. The most outstanding of these were:

|  | No. of Patients |
|--|-----------------|
| Arteriosclerosis .....                       | 61              |
| Myocardial and valvular lesions .....        | 28              |
| Pulmonary tuberculosis .....                 | 15              |
| Chronic bronchitis and emphysema .....       | 65              |
| Anæmia (hæmoglobin below 60 per cent.) ..... | 61              |
| Obesity .....                                | 30              |
| Diabetes .....                               | 10              |
| Nephritis .....                              | 4               |

*Nature of Operation.*—The types of operation in this series of cases were as follows:

|   |     |
|---|-----|
| Stomach (126 gastrectomies) .....             | 154 |
| Intestinal (including appendicectomies) ..... | 94  |
| Liver and biliary passages .....              | 72  |
| Hernioplasties .....                          | 60  |
| Exploratory laparotomies .....                | 39  |
| Kidney and bladder .....                      | 39  |
| Rectal and recto-sigmoidal resections .....   | 26  |
| Extremities (lower) .....                     | 8   |
| Gynæcological .....                           | 3   |
| Splenectomies .....                           | 2   |

*Untoward Reactions.*—In this series of cases, untoward symptoms of a transitory nature, *i.e.*, nausea, vomiting, shallow respirations, which had no effect on the patient's condition or the efficacy of the anæsthesia, were not accurately enough observed to be recorded. Instances of more pronounced reactions were observed in twelve cases. These reactions were evidenced chiefly by the signs and symptoms of shock.

*Complications.*—Which were directly attributable to the spinal anæsthesia were: 1. Aseptic meningitis, one case; 2. Pyocyaneus meningitis, one case; 3. Transverse myelitis, one case. Complications in which spinal anæsthesia was possibly contributory:

1. Suppression of urine, two cases.

Suppression of urine is probably the result of marked drops in blood-pressure in patients with long-standing hypertension. The kidneys which are accustomed to secrete at a high pressure fail to secrete at such a low level.

2. Vascular complications.—a. Phlebitis, four cases; b. Hemiplegia, three cases.

It is difficult to state how much of a rôle spinal anæsthesia plays in the incidence of vascular complications. We do not know what the incidence of vascular complications would be in a similar series of cases of general anæsthesia. It is possible, that with the usual drop in blood-pressure and slowing of the blood-stream, thromboses would be relatively more frequent.

*Pulmonary Complications.*—1. Pneumonia, twenty-one cases; 2. Pulmonary infarct, two cases; 3. Pulmonary emboli, two cases.

The high incidence of pneumonia, twenty-one cases (4.2 per cent.), was somewhat of a surprise. These pneumonias were all verified either by X-ray or post-mortem examination. We soon learned that spinal anæsthesia did not prevent post-operative pulmonary complications.

*Deaths.*—Deaths which were undoubtedly due to spinal anæsthesia: 1. Pyocyaneus meningitis, one case, case No. 306234 above; 2. Transverse myelitis, one case, case No. 300122 above; 3. Spinal anæsthetic shock, one case.

In this last case, Hosp. No. 306931, the patient was a woman, sixty-nine years of age, who was admitted with a three-day history of generalized abdominal pain gradually localizing into the right lower quadrant. There were no similar previous attacks. Physical examinations showed an obese woman with general signs of senility, but who seemed to be in good general condition. There was deep and rebound tenderness over McBurney's point, and rectal tenderness on the right side. The blood-pressure was 134/90. A spinal anæsthesia was given, 120 milligrams of neocaine between the first and second lumbar vertebræ. Five minutes after the operation had started, the patient ceased breathing and the pulse could not be obtained. In spite of all restorative measures—intravenous, cardiac massage and intracardiac adrenalin—she did not respond. There was no post mortem examination.

Deaths in which spinal anæsthesia was possibly a contributory cause:

1. A case of partial colectomy for carcinoma of the colon, operation lasting over two hours.

2. A seventy-eight-year-old man subjected to amputation through the mid-thigh for arteriosclerotic gangrene of the foot. Condition became poor soon after injection of spinal anæsthetic. Duration of operation, eighteen minutes; death at end of twenty-four hours.

3. Case of suppression of urine cited above under the heading of complications.

4, 5, 6. Three cases of hemiplegia, which came on one and three days after operation. The patients died three, seven and ten days after operation. Deaths undoubtedly not due to spinal anæsthesia—seventy-three.

## SUMMARY

1. This series of 497 cases of spinal anæsthesia was, for the most part, a selected one, spinal anæsthesia being used in cases in which there was a contraindication to general anæsthesia, or cases in which the major operative procedures, usually abdominal, could be more easily carried out. We hope to report a more representative series in the future.

2. No relation could be determined between the changes in blood-pressure and the level of injection of the anæsthetic (usually neocaine in the dosage of 120 milligrams).

3. There was no anæsthesia in eight cases (1.6 per cent.).

4. The number of cases in which the spinal anæsthesia had to be supplemented by general anæsthesia was 163 (32.8 per cent.). We have more recently found that the number of supplementary anæsthesias can be cut down by using larger doses of the drug, neocaine.

5. Pronounced reactions on the operating table, which were evidenced chiefly by the signs and symptoms of shock, occurred, for the most part, in patients in advanced years who showed evidences of arteriosclerosis and myocardial disease, or in those cases of cachexia or intoxication from some debilitating disease.

6. Cases of hypertension may develop suppression of urine as a result of marked drops in blood-pressure when not overcome.

7. There was a relatively high incidence of post-operative pneumonias—twenty-one cases (4.2 per cent.).

8. There was one toxic spinal anæsthetic death (0.2 per cent.) the other two deaths being due to errors in technic which are avoidable.

*Conclusion.*—Spinal anæsthesia is an excellent anæsthesia because of the great technical advantage to the surgeon and the relatively little upset of general body metabolism, but its dangers should be clearly understood, and its indiscriminate use discouraged.



# TRANSACTIONS

## OF THE

# NEW YORK SURGICAL SOCIETY

STATED MEETING HELD NOVEMBER 12, 1930

The President, DR. EDWIN BEER, in the Chair

### CONGENITAL ABSENCE OF SIGMOID AND RECTUM, COLOSTOMY

DR. SETH M. MILLIKEN presented a child five years of age who was born at 8 P.M. October 11 and first seen by him about 10 A.M. October 12, 1925. The child seemed normal except for absence of anus. At the anal site there were two projecting skin tabs but no perforation of the skin. There seemed to be some impulse against the perineum when the baby cried. A scalpel was introduced with no result and finger inserted between tuberosities failed to palpate descending bowel. Pelvis apparently empty. A weak barium mixture was taken in teaspoon doses every two hours for twelve hours. X-ray October 13 showed normal small intestine with barium as far as the cæcum and gas distending the large intestine as far as a smooth caput implanted in the left iliac fossa. Colostomy was then (October 13) performed through the left rectus. Finger inserted found lower extremity of descending colon completely closed and attached to left iliac fossa. The sigmoid and rectum were absent. The baby was sent home two days after operation and has made satisfactory progress to the present.

There is now herniation of the descending colon mucosa of about  $2\frac{1}{2}$  inches; the colostomy ring is slightly large. Finger may be inserted distally to the iliac fossa. The boy has not yet learned to regulate evacuations and the moisture from blind end is annoying.

DR. HENRY W. CAVE remarked that at times it is exceedingly difficult to determine the exact site of the atresic band even though the anus be present and not merely a dimpling. It is difficult to determine whether the obstruction from the atresia is in the large or small bowel, as usually the child is so young and the distention so marked. Where there is a doubt, a small amount of barium may be instilled into the rectum, and then take X-rays. A catheter inserted into the rectum to see whether it is patent as far as the sigmoid gives often unreliable information. A few years ago a child four years of age was referred to him from the Nursery and Childs Hospital with complaint of obstipation, nausea and vomiting since birth. The father had tried unsuccessfully to give it an enema. It was then taken to the Nursery and Childs Hospital where two internes had tried to insert a No. 20 French catheter but this was admitted only to 6 centimetres. The child was then brought from the Nursery and Childs Hospital to the Roosevelt Hospital where three of the interne staff and two of the attending staff attempted unsuccessfully to insert a French catheter up into the bowel. The insertion of the little finger was stated to have divulged a blind pocket of the rectum so

## OBLIQUE FRACTURE, MIDDLE FEMUR: TRACTION SUSPENSION

that an atresic band was thought to exist somewhere in the recto-sigmoid or sigmoid. However, to the surprise of everyone when a left rectus incision was made there was no absence of the sigmoid nor even an atresic band of the sigmoid, but there was found an atresic band about 4 inches in length and about the size of an ordinary shoe lace in the last portion of the ileum. An ileostomy was immediately done. The child made a satisfactory recovery from this first operation and sixteen days later—after a barium enema had shown the patency of the large bowel—an ileocolostomy was done; the ileum proximal to the ileostomy wound was anastomosed to the transverse colon. The child, however, died four days later from a broncho-pneumonia. An autopsy revealed: Bilateral broncho-pneumonia, the ileocolostomy anastomosis secure and no evidence of peritonitis.

DR. FREDERIC W. BANCROFT said that the finding of a gas bubble in the terminal segment is often of considerable value. In two cases in which he had waited thirty-six hours after birth for an X-ray, by placing a metal indicator on the anal dimple and observing the bubble of gas in the terminal bowel segment it was possible to gain some idea of the distance between the two by a lateral X-ray plate. It was necessary in one case to raise the buttocks, in order to aid gravity. While in many cases it may be necessary to do a laparotomy to determine the procedure, in the cases where the bubble and the indicator are near each other this procedure may be avoided.

## OBLIQUE FRACTURE, MIDDLE FEMUR: TRACTION SUSPENSION

DR. SETH M. MILLIKEN presented a man, thirty-six years of age, who was brought to the French Hospital after having been struck by a taxicab. He was admitted at 10.30 P.M. November 14, 1929. Besides a slight scalp wound there was a fracture of the left thigh with shortening of  $3\frac{1}{2}$  inches, the fragments projecting under the skin.

Suspended traction with Thomas splint and Pierson leg piece, knee in 90 degrees flexion, was immediately applied with a total of 43 pounds, traction weight (Fig. 1). X-ray following morning (Fig. 2), showed good reduction which gradually improved. Weight diminished as soon as fragments were in alignment, which occurred the fourth day. Union prompt, function slowly regained. Was discharged walking on crutches March 28, 1930, able to bear full weight on that side. Last seen October 17, 1930, at which time he had resumed his usual occupation and was walking without limp. Measurement showed no difference in two extremities (Fig. 3).

Doctor Milliken said he was presenting this patient to explain the purpose of the flexed knee traction in fractures of the femur. By flexing the knee the distal part of the quadriceps muscle is drawn downward so that any part of the muscle which may have been engaged on the proximal fragment is freed and the bone ends thus cleared may engage with the distal fragment which by the traction is aligned with the proximal fragment both by the direction of pull and by the compression of the encasing muscles. Traction with the leg in extension does not thus relax the distal portion of the quadriceps and interposition of soft parts is less easily avoided. The elevated

foot of the Gatch bed gives the patient a firm and comfortable counter pressure point making the full force of the weight exert traction on the lower fragment without displacing the patient. Pressure on the back of the calf is relieved by extending the leg from time to time, which should not be done until perfect reduction has been accomplished. The posterior half of the Thomas ring is unnecessary and may be a source of danger as the upper fragment will rest upon it and be thrown forward into a flexed position making it necessary to elevate the distal fragment an undue amount. Without the posterior half of the ring the upper fragment rests on the mattress, all counter pressure being borne by the buttocks. If the reduction by attachment to the skin only is not complete tongs are promptly attached to the

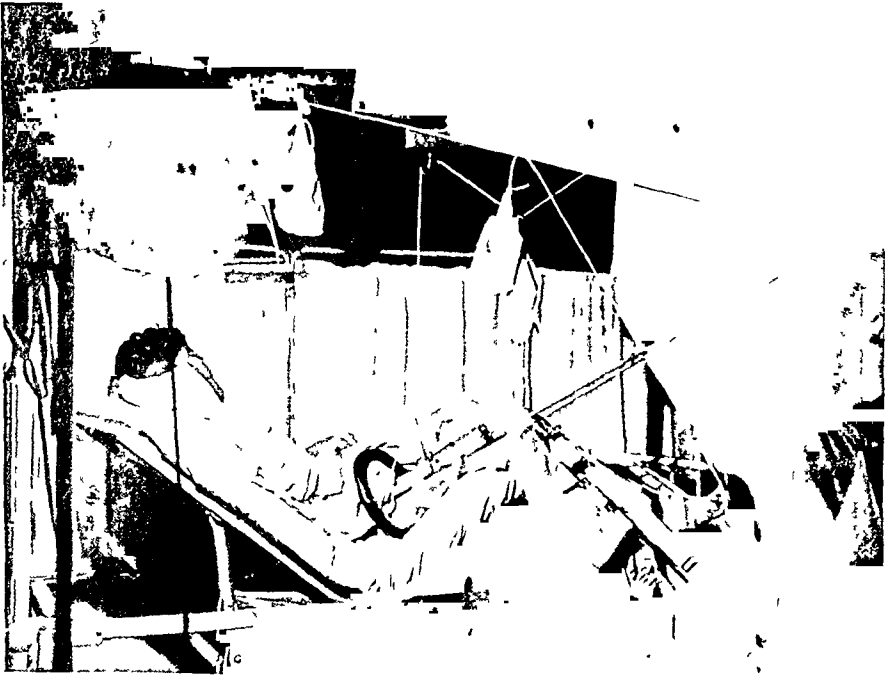


FIG. 1.—Illustrating suspended traction for supracondylar comminuted T fracture. The flexed leg with the traction on the lower end of the Thomas splint accomplishes the reduction. Voluntary motion is allowed as desired.

condyles, which avoids any danger of skin necrosis at upper part of leg. It is particularly important to apply adequate weight at the outset so that the muscles may be stretched before they have become contracted.

DR. KIRBY DWIGHT said he had used this method of traction in a number of cases, and the results had been very satisfactory and he had considerable confidence in it. He did not rely, however, entirely on skin traction or pressure against the back of the calf. He preferred to use skeletal traction on the lower end of the femur and skin traction on the leg. The great advantage of this form of treatment lies in the fact that the patient can have first passive and later active motion of the knee-joint, without altering the tension at the line of fracture, and consequently with much less pain. That is the principal advantage, and the second is that skin traction on the leg is much

## RELATION OF WELCH BACILLUS TO APPENDICITIS

more effective when direct pressure on the calf of the leg is used to supplement it.

DOCTOR MILLIKEN, in closing the discussion, said that he also put in tongs or a nail if there was difficulty in obtaining reduction of over-riding. If skin traction did not reduce the over-riding in twenty-four hours, skeletal traction was put on.



FIG. 2—Lateral view after twelve hours' traction showing correction of  $8\frac{1}{2}$  inches over-riding, at which time weight was reduced to 25 pounds.

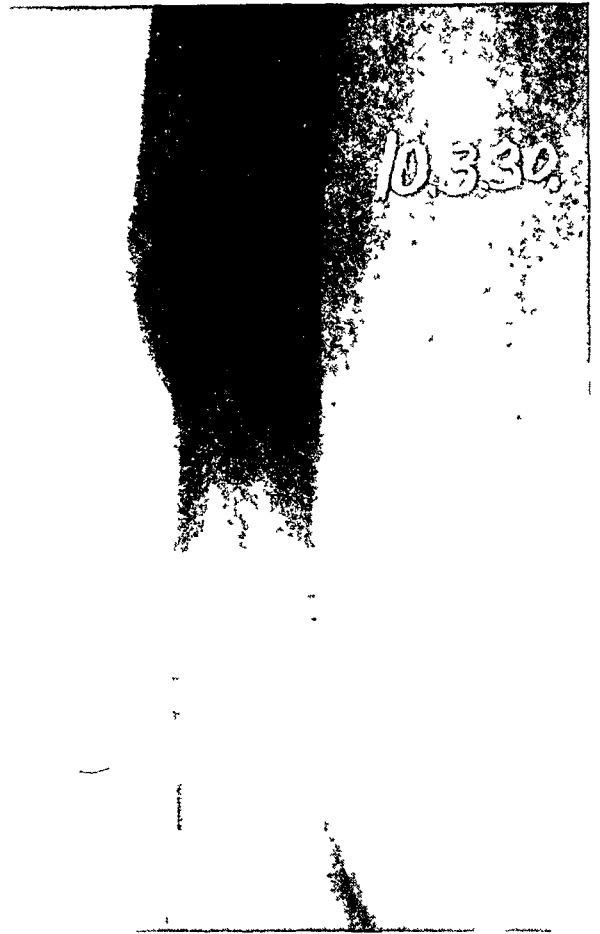


FIG. 3—Lateral view showing good weight-bearing alignment with small callus.

### THE RELATION OF THE WELCH BACILLUS TO APPENDICITIS AND ITS COMPLICATIONS

DR. JOHN E. JENNINGS read a paper with the above title for which see page 828.

DR. FRANK L. MELENEY remarked that four years ago a group on the surgical staff of the Presbyterian Hospital undertook to study the problem of peritonitis because of its extreme surgical importance. They were naturally greatly interested in the work of Williams and Heyde and others whom Doctor Jennings has mentioned and read with interest his own publications and those of Weinberg which appeared two years ago. Their chief criticism of the bacteriology in these reports is that cultures were made from the lumen or the wall of the appendix which was removed at operation and conclusions

were drawn from these findings. It would have been more to the point to study the peritoneal fluid, a part of which is always left in the abdominal cavity after operation. They made cultures of peritoneal fluids and then tried to correlate their findings with the clinical aspects of the case both before and after operation. In their laboratory work, although they tried to have no preconceived notions, they laid particular stress upon recovering the anaërobes because of their prevalence in the intestinal tract and because of the emphasis placed upon them by recent workers. An anaërobic technic was used which they have found satisfactory in culturing the well-known anaërobes and believe that their results with regard to *B. welchii* approximate closely the incidence of that organism in the peritoneal exudates of their cases. He would confine himself to that portion of their data which pertains to the significance of *B. welchii*.

I.—Their series included 106 cases of peritonitis of which 76 were due to appendicitis and 30 to other causes. Seventy-one of these cases yielded one or more specimens of bacteria. *B. welchii* occurred twenty-seven times or 38 per cent. It never occurred alone. It was always in association with other organisms and it was much more common when many different species were present, than when only two or three species were present but the percentage of mortality in these two groups was exactly the same. In the smaller group *B. coli* was five times as common and the green streptococcus twice as common as *B. welchii*; while in the prolific group *B. welchii* more nearly approached the others. These three were the organisms most commonly found. See Table I.

TABLE I

|                               | Number of species cultured |     |     |
|-------------------------------|----------------------------|-----|-----|
|                               | None                       | 1-3 | 4-6 |
| Total number cases.....       | 35                         | 40  | 31  |
| Non-hæm. <i>B. coli</i> ..... | —                          | 32  | 30  |
| Green strept.....             | —                          | 14  | 21  |
| Hæm. <i>B. welchii</i> .....  | —                          | 6   | 21  |
| Mortality.....                | 0                          | 22% | 22% |

II.—The correlation of the bacteriological findings with the clinical course was more significant when the cases were divided into three groups according to the extent of peritoneal involvement. The only features specially notable in this connection are the percentage incidence of the organism and the percentage mortality in each group. Table II shows that the percentage of incidence, as well as mortality, with *B. welchii* was almost always less than with the other two common organisms.

III.—When the occurrence of these organisms in cases of appendicitis was compared from the standpoint of the severity of symptoms on admission,

# RELATION OF WELCH BACILLUS TO APPENDICITIS

TABLE II

|                                     | Percentage |       |               |       |            |       |
|-------------------------------------|------------|-------|---------------|-------|------------|-------|
|                                     | B. coli    |       | Green strept. |       | B. welchii |       |
|                                     | Incid.     | Mort. | Incid.        | Mort. | Incid.     | Mort. |
| Acute local peritonitis . . . . .   | 28         | 0     | 11            | 0     | 13         | 0     |
| Acute diffuse peritonitis . . . . . | 75         | 28    | 42            | 17    | 31         | 17    |
| Peritoneal abscess . . . . .        | 96         | 17    | 65            | 13    | 44         | 4     |

the number of post-operative complications and the mortality, it was found that those cases yielding *B. welchii* were not appreciably sicker on admission and had only a slightly greater number of complications. The mortality was exactly the same as in the *B. coli* group and definitely less than in the streptococcus group. See Table III.

TABLE III

| Total number                 | B. coli |    | Green strept. |    | B. welchii |    |
|------------------------------|---------|----|---------------|----|------------|----|
|                              | 46      |    | 24            |    | 15         |    |
|                              | No.     | %  | No.           | %  | No.        | %  |
| Moderately ill . . . . .     | 37      | 80 | 19            | 79 | 11         | 73 |
| Severely ill . . . . .       | 9       | 19 | 5             | 21 | 4          | 27 |
| Few complications . . . . .  | 38      | 82 | 20            | 83 | 11         | 74 |
| Many complications . . . . . | 8       | 17 | 4             | 17 | 4          | 26 |
| Recovered . . . . .          | 40      | 87 | 19            | 79 | 13         | 87 |
| Died . . . . .               | 6       | 13 | 5             | 21 | 2          | 13 |

In this table, of course, there is overlapping of cases because of the simultaneous occurrence of these organisms.

IV.—The difference between a monomicrobial and a polymicrobial infection is seen when combinations of these organisms are compared with one of them alone. *B. coli* was the only one of these three which occurred alone. The conditions were very much worse when the other organisms were present also. Although the presence of *B. welchii* may have been a factor in increasing the estimate of the severity of the illness before operation, it did not increase the mortality at all. See Table IV.

TABLE IV

|   | Totals | Severity |       | Result |      |
|---|--------|----------|-------|--------|------|
|   |        | Mod.     | Grave | Recov. | Died |
| <i>B. coli</i> alone . . . . .                                    | 9      | 89%      | 11%   | 100%   | 0    |
| <i>B. coli</i> and g. strept. without <i>B. welchii</i> . . . . . | 26     | 81%      | 19%   | 69%    | 31%  |
| <i>B. coli</i> and g. strept. with <i>B. welchii</i> . . . . .    | 22     | 55%      | 45%   | 73%    | 27%  |

V.—When the different types of appendicitis are compared to estimate their relative importance it is found that the acute appendicitis cases with acute local peritonitis but without perforation were mild, had few sequelæ and all recovered, although two of these cases yielded *B. welchii*. When there was gangrene without perforation, likewise the cases were mild, had few sequelæ and all recovered. In these cases *B. welchii* was never found in the peritoneal exudate, suggesting that while it may have played a part in the production of the gangrene it did not pass through the wall and multiply in the peritoneal cavity. When perforation occurred, large numbers of different species of bacteria were cultivated from the fluid. *B. coli* was found in every case but *B. welchii* in less than half of them suggesting either that it was not present in the lumen (which is not likely) or that it could not maintain itself in the peritoneal cavity. In this group, *B. welchii* occurred more than twice as many times in the abscess cases as in the diffuse cases but the mortality was greater in the latter group. These points are brought out in Table V.

TABLE V

|                         | Ac. inflam.<br>without<br>perforation | Gangrene<br>without<br>perforation | Perforation;<br>diffuse<br>peritonitis | Perforation<br>with<br>abscess |
|-------------------------|---------------------------------------|------------------------------------|--|--------------------------------|
| Number of cases.....    | 31                                    | 8                                  | 11                                     | 12                             |
| Moderately ill.....     | 31                                    | 8                                  | 6                                      | 9                              |
| Severely ill.....       | 0                                     | 0                                  | 5                                      | 3                              |
| Few complications.....  | 31                                    | 8                                  | 2                                      | 11                             |
| Many complications....  | 0                                     | 0                                  | 9                                      | 1                              |
| Recovered.....          | 31                                    | 8                                  | 8                                      | 10                             |
| Died.....               | 0                                     | 0                                  | 3                                      | 2                              |
| <i>B. coli</i> .....    | 5                                     | 5                                  | 11                                     | 12                             |
| Green strept.....       | 2                                     | 2                                  | 6                                      | 9                              |
| <i>B. welchii</i> ..... | 2                                     | 0                                  | 3                                      | 7                              |

When lesions of the small and large gut were considered it was found that *B. welchii* were present in all three cases of perforated ileum and all were fatal. It was likewise present in all of the five cases of perforated colon and all but one recovered. This patient was almost moribund on admission. This suggests that it is not so much the nature of the organisms as the dosage of these organisms or the presence of irritating intestinal juices that determines the fatal outcome.

When viewed from every angle, these studies seem to show that the severe cases of peritonitis are polymicrobial, that *B. coli*, green streptococcus and *B. welchii* are the commonest organisms present. The importance of any one of these species, in the series, seemed to depend more upon its prevalence than upon its virulence. All of the evidence seemed to show that *B. welchii* *per se* did not materially increase the severity of the disease or increase the chance of a fatal outcome.

When they began this study, they gave serum to unselected cases yielding *B. welchii*. Two out of five, or 40 per cent. died. As soon as these results

## RELATION OF WELCH BACILLUS TO APPENDICITIS

began to be apparent, the use of serum was given up. Of the untreated twenty-two cases yielding *B. welchii*, five died or 23 per cent.

They do not believe that *B. welchii* antitoxin is going to be the solution of the problem. They believe that the only hope of further success, aside from earlier operation, lies in a study of the symbiosis of these bacteria and the rôle played by the intestinal digestive juices and the faecal foreign bodies.

DR. HENRY H. M. LYLE remarked as to the use of serum for gas gangrene, that undoubtedly the serum has been improved since the war. In the early years he was in charge of the hospital in which some of the original work referred to was carried on and where many tests of the serum were made. No apparent results were obtained. In the later years of the war with supposedly improved serum he still was unconvinced of its value.

The mere finding of *B. welchii* in a wound does not necessarily imply a severe gas gangrene; it was often found in war wounds which ran a mild course. Other factors such as the associated bacteria, the condition of the tissues, the blood and nerve supply were as important factors in determining the severity of the case as the presence of *B. welchii*. It was often found in wounds but rarely in the blood. Yet at autopsy gas infection of liver and other organs were found. Doctor Lyle has an impression that it was in the circulation more often than the laboratory reports would indicate.

Doctor Lyle, in 1916, showed before the surgical section of the Academy of Medicine a specimen of heart and liver tissue infected with gas bacilli with the absence of local infection. This French soldier had been wounded on the left thigh by a shell fragment. At the time of the entrance to the hospital the patient had a perforating wound of the upper left thigh. The wound was débrided and Carrel treatment started—no shell fragment was found. The patient insisted that the fragment had not been removed at the front. X-ray at level of anterior-superior spine showed no foreign body. The wound remained clean and no bacteria were found in the smears. On the third day the patient began to show evidence of a generalized gas infection—no local signs—on the fourth day he died suddenly. At autopsy a clean closed wound of the right femoral vein was found. In the right ventricle a small shell fragment was found. Attached to it was a portion of the uniform. The shell had entered the femoral vein and migrated to the right ventricle. The source of the blood infection was the small portion of the uniform attached to the shell. The heart with shell fragment in place was sent to the Army Medical Museum. This was the first case on record of migration of shell fragment to the heart. The Grandgerara case was a shrapnel bullet which, although reported before the above case, happened after it.

DR. ROBERT T. MORRIS said that his feeling in regard to the serum was like that of Doctor Lyle. Doctor Morris also considered that it was very difficult to tell which of the invading microorganisms is the dominating one, unless one made cultures, as Doctor Jennings did and as they did at the Presbyterian Hospital, in order to determine the relative virulence of each



strain. Unless one does that, it is difficult to decide their relative importance. Many years ago the speaker called attention to the fact that surgeons were overlooking anaërobes in making examinations of cases of peritonitis. That was probably because the methods now prevailing for finding them were not then in use. Nowadays one who goes after any particular bacterium finds it by special methods. The question of whether Welch's bacillus is present in these cases or not is of small importance, compared with the basic causative fact that there is invasion of the terminal artery of the appendix or of its branches. When these are plugged with the exudate of endarteritis, the circulation of the appendix is cut off partly or wholly, and any bacteria that come along will get in their work. The extent of plugging of the terminal artery determines the degree of gangrene as a rule. A microbe capable of causing gangrene may be nothing more than a saprophyte in a given case. Consequently a serum made from that microbe would have a highly speculative place in the treatment of appendicitis—might do harm.

DR. JOHN DOUGLAS said that Doctor Jennings' paper and the remarks of Doctor Meleney and Doctor Lyle seemed to him to indicate that it depends more on whether these anaërobes are growing and are toxic, than whether they are present in cultures of the appendix. He remembered operating on a case a few years ago in a woman fifty-three years of age for abscess of the appendix. There was no reason why she should not have got well on drainage, but she developed a particularly extensive gangrenous infection of the abdominal wall. This was shortly after Doctor Jennings had first reported some of his cases treated with serum. Doctor Douglas gave his patient perfringens antitoxin and firmly believed that he thereby saved her life. Doctor Douglas cited another case which illustrated his idea of the lack of value of culturing for anaërobes in a fulminating case. The operation was a gastric one. The man, apparently doing well, became very ill and died in thirty-six hours. The wound showed gas bacillus infection and the peritoneal cavity and liver were full of Welch bacilli.

DR. SEWARD ERDMAN said he was sure that surgeons cannot be entirely satisfied with the present results of surgery for appendicitis. The patients die too frequently. The general percentage of mortality is 10 per cent. for the acute cases, and somewhere between 5 per cent. and 10 per cent. is the average mortality from the best hospitals. That is nothing to be proud of. And yet this evening, listening to the general discussion, one got the impression that this must be accepted and cannot be changed. But the speaker was optimistic. He believed that some method will be evolved which will help these patients. Consequently he was very glad to hear Doctor Jennings looking forward and holding out hope that one more method may be added to our armamentarium, that will be helpful and will lower the mortality. The work done at the Presbyterian Hospital would seem to negative the claim of Doctor Jennings, but one cannot but believe that there are cases in which the serum should be given a fair trial.

DR. CHARLES L. GIBSON remarked that he had been interested in the possibility of reducing the appendicitis mortality, even to a very slight extent, by advocating some such treatment as that described by Doctor Jennings, especially anti-gangrenous serum. There is a very general skepticism against vaccines and antitoxins, and the speaker himself had been apathetic until he learned from Doctor Michel, of Nancy, France, that he had reduced the mortality about 40 per cent. in cases of gangrenous peritonitis, by the use of the antitoxin which was furnished by the Pasteur Institute. The last time Doctor Gibson went abroad he obtained some of this vaccine, but found it could not be imported. In the use of it on his service at the New York Hospital, he had encountered the same skepticism. His assistants would not use it. Even if the serum saves only one life in a thousand, that would be worth while. Personally, the speaker believed the treatment was valuable.

DR. WALTER A. SHERWOOD stated that his own experience in the use of perfringens serum in similar conditions had been limited to about a dozen cases. In these it had been used more or less empirically and without the aid of complicated bacteriological studies. It had been used by him on the basis of clinical observation only and it was impossible to evaluate the results in such a small series of cases. Several of the patients had severe serum reactions. A practical difficulty is the present expense of this product as supplied by the drug firms and commercial laboratories.

DR. JOHN F. CONNORS said that he had had considerable experience with the use of serum during the war in France and he came home with the idea that its value in the treatment of gas infections was questionable. However, after reading the article by Williams, of London, about the use of serum in cases of appendicitis with perforation and peritonitis as well as in cases of intestinal obstruction he thought it was worth a trial. The serum for this trial was supplied by the Lederle Laboratories. It was used in twelve cases of perforated appendix with peritonitis and all these patients recovered. It was tried in eight cases of intestinal obstruction without a mortality. The question, however, arose among the staff as to what part early operation and spinal anæsthesia played, as it undoubtedly played some part. The one great obstacle is the high cost and in a municipal hospital it is difficult to get the city to purchase the serum. The mortality in appendicitis with perforation and peritonitis is still too high and if this serum can be added to the facilities for helping to reduce this mortality, it is too valuable an adjunct to be overlooked.

DOCTOR HERZFELD, of Buenos Aires (by invitation), said that vaccine had been used in his hospital as a routine measure in all cases of gangrenous appendicitis for the last three years, and they had found it very satisfactory. It was manufactured by a dependency of the Government, and it was used in doses of 30 cubic centimetres diluted in 250 cubic centimetres normal saline solution injected at one time. This dose is repeated in twelve-hour

intervals if and as symptoms require. The mortality since the institution of its use had been greatly reduced.

DOCTOR JENNINGS, in closing the discussion, said that after ten years' intensive use of the only serum obtainable, it had been felt that there were a sufficient number of successes to justify going on with its use in cases equally in jeopardy. The speaker did not criticize Doctor Meleney's excellent report of the work done at the Presbyterian Hospital, but wished to point out that if he would study the article of Weinberg, published in 1928, who carried this work further, he would probably elaborate his technic as Weinberg has done. Weinberg has done the same work with fuller elaboration and has come to the conclusion that this serum is very useful. The whole article will help to clarify the situation, as will the work of Michel. The way in which Doctor Jennings attempted to attack this problem was as follows: Without a complete anaërobic laboratory, the best thing to do is to look for one or two or three bacteria and attempt not to miss the tree on account of the forest. No attempt is made to make a census of the flora of the intestine of the case, which few laboratories are able to accomplish, but an effort is made to see if one thing can be found which can be recognized. That can be done with the simple guinea-pig technic. Only by that means of attacking the essential organisms in the large intestine, one at a time, will it be possible to come to any real opinion of their rôle. American serum has been found very useful in severe cases, if like any other serum it be given early and enough be given. The speaker did not know whether antitoxin was invariably useful, but if it be used early in cases where the Welch bacillus is recognized, it will cut down the mortality.

STATED MEETING HELD NOVEMBER 26, 1930

The President, DR. EDWIN BEER, in the Chair

#### BLEEDING DUODENAL ULCER: PARTIAL GASTRECTOMY

DR. RICHARD LEWISOHN presented a man who at the time of his admission to Mt. Sinai Hospital, June 3, 1926, was forty-nine years old. This patient had been suddenly seized five days previously with a feeling of faintness and vomited a large amount of blood. His condition had become gradually worse. Preceding this attack he had had a long history of epigastric distress which was relieved by bicarbonate of soda. He was often nauseated. His stools during the last few days were tarry. On admission his blood-pressure was 85/48 and his hæmoglobin 20 per cent. An immediate citrate transfusion was given and another was given about twelve hours later. During the four days following these two transfusions his hæmoglobin rose to about 40 per cent. He was placed on a Sippy diet, his condition gradually improved, but his hæmoglobin did not go up beyond the figure quoted. A pre-operative transfusion was given on July 12 and a partial gastrectomy (Billroth II with Hofmeister anastomosis) was performed July 14. The ulcer, which was situated in the first part of the duodenum about 2 centimetres beyond the pylorus, was removed with the distal half of the stomach. The specimen showed an ulcerated area in the first part of the duodenum with

an open vessel at the bottom of the ulcer. This open vessel evidently had caused the bleeding. In addition to this a diverticulum was present just below the ulcerated area. The patient made an uneventful recovery and has gained 30 pounds since his operation. He still has considerable acidity in his stomach, his curve going up to 60 for free acid and to 76 for total acidity. He feels perfectly well.

#### BLEEDING DUODENAL AND GASTROJEJUNAL ULCER: SUBTOTAL GASTRECTOMY (FINSTERER OPERATION)

DOCTOR LEWISOHN presented also a patient who was first admitted to Mt. Sinai Hospital in 1918. A gastro-enterostomy was then performed for a duodenal ulcer by another surgeon. The patient felt perfectly well up to seven weeks previous to his second admission in 1923. He then experienced attacks of pain about three hours after his meals. Two days previous to his admission he had a very severe attack of pain. At the time of his second admission he had free acidity of 33, and total acidity of 60. Five days after his admission to the hospital he suddenly felt dizzy and his stools contained a large amount of blood. His hæmoglobin dropped to 29 per cent. A citrate transfusion was given and the hæmoglobin rose to 43 per cent. The X-ray which had been taken three days previously, before the hæmorrhage started, showed a gastrojejunal ulcer with a large residue in the stomach, even after nine hours. He was explored by the same surgeon who noted the following findings: "The stomach was adherent, dilated and could not be delivered. An infiltrated mass was felt at the site of the stoma, probably a gastrojejunal ulcer. A small, hard mass was felt near the pylorus about 1 centimetre in diameter apparently with a crater. The pylorus was adherent to the gall-bladder. This adhesion was carefully divided and a small piece of tissue in this area was excised for pathologic examination. The opening in the intestine was closed with Pagenstecher and omentum was sewed over it. Pathologic examination of the specimen showed œdematous connective tissue and normal intestinal mucosa."

Another transfusion was given immediately after the operation. The hæmoglobin dropped from 43 per cent. to 18 per cent. Another transfusion was given January 12, 1923. The bleeding gradually stopped and an attempt was made to treat this patient medically after the wound had healed by primary union. He left the hospital March 8, 1923.

On September 3, 1923, he was readmitted stating that his symptoms recurred about one week before his readmission. On the day of readmission he vomited about 8 ounces of dark red blood. At this time his hæmoglobin was 25 per cent. Two days later it had dropped to 20 per cent. and a citrate transfusion was given. However, the bleeding persisted and the patient appeared in a most desperate condition. He was pale and was so weak as to be unable to sit up in bed. After another transfusion by the Unger method the patient was operated on September 15, 1923. A large, hard, indurated gastrojejunal ulcer, the size of a silver dollar, completely surrounding the gastroenterostomy stoma was found. The stomach was large and hypertrophied. A crater ulcer was felt between the first and second parts of the

duodenum which was very adherent to the pancreas. The stomach and duodenum were adherent to the gall-bladder and liver. The adhesions between the duodenum and gall-bladder were divided. The duodenum appeared to be quite movable in all parts, except at the base where the ulcer described above was adherent to the head of the pancreas. By careful dissection the gastroenterostomy stoma was entered and the jejunum was separated from the stomach. The opening in the jejunum was closed in two layers. The ulcerated area in the gastroenterostomy stoma was carefully dissected away from the colon, to which it was very adherent. The patient's condition at this time was not good. The pulse was so rapid as to be imperceptible at times. It was thought that removal of the duodenal ulcer would necessitate considerable manipulation of the pancreas and would be followed by marked shock and so it was decided to perform the Finsterer type of subtotal gastrectomy, removing the stomach with the gastrojejunal ulcer, dividing the stomach just beyond the pylorus and leaving the ulcer of the duodenum *in situ*. In order to expedite the operation a Murphy button was used for the anastomosis between the stomach and jejunum. The patient made a good recovery from this operation aside from a partial paralysis of the right arm which subsided under electric treatment. He left the hospital October 29, 1923. He has been perfectly well since his operation and has gained 50 pounds in weight. An Ewald test meal in 1926 showed free acid 0, total acidity 20.

#### PROSTATECTOMY IN A NONAGENARIAN

DOCTOR LEWISOHN presented a man, ninety-four years of age, who had been admitted to Mt. Sinai Hospital in September, 1928, with an acute suppurative tenosynovitis and which required multiple incisions. While the patient was in the ward he developed an acute urinary retention which was improved by repeated catheterizations. Rectal examination showed a large prostate. In view of the patient's age operation was not deemed advisable and the patient was sent home. He returned three days later with a marked acute urinary retention. His blood urea was 18. He was treated with a permanent catheter for about one week. A bilateral vasectomy was done September 27, 1928. One week later the first stage of a suprapubic prostatectomy was performed under local anæsthesia. One week after the suprapubic drainage, the prostate was removed under sacral and parasacral anæsthesia. The patient made a perfect recovery and is in perfect health at present, two years after the operation.

Doctor Lewisohn stated that this case was shown in order to demonstrate that even in very advanced age prostatectomy can be performed with great benefit to the patient. Doctor Lewisohn stated further that although he had not looked up the records he thought that this was probably the oldest patient ever subjected to a prostatectomy at Mt. Sinai Hospital.

#### RESULTS IN SUBTOTAL RESECTION OF THE STOMACH

DR. THOMAS H. RUSSELL presented four cases upon whom he had operated during the past year for hæmorrhage from gastric or duodenal ulcers, as they may be of interest in connection with Doctor Hinton's paper later to be read.

## RESULTS IN SUBTOTAL RESECTION OF THE STOMACH

The first case, a man, fifty-seven years old, admitted to St. Francis Hospital November 20, 1929, complaining of pain in the epigastrium. At first this had been relieved by taking food, but later food did not give relief. On February 4, 1924, the patient was operated upon by Doctor Russell at the Post-Graduate Hospital. At that time a large ulcer about the size of a twenty-five cent piece was found on the upper posterior surface of the first portion of the duodenum. The surrounding tissues were so infiltrated and cedematous that it was deemed unwise to attempt a subtotal resection at that time. After the gall-bladder had been dissected from the adherent duodenum it was removed in the usual way. An attempt was made to remove the ulcer by a transduodenal incision, but finding it impossible the base of the ulcer was cauterized. A posterior gastroenterostomy was performed at the junction of the proximal and middle two-thirds of the stomach. This site was selected in order that the distal half of the stomach could be removed at a subsequent operation if necessary. The appendix was also removed. Unexpectedly, this patient improved very much and while he did not gain appreciably in weight his general appearance was better and he admitted that he felt very markedly improved. However, it was necessary for him to consult Doctor Russell every few months on account of recurrence of gastric symptoms.

In the fall of 1927 he was riding through Central Park one evening when a taxicab collided with the one in which he was riding. Soon after the accident he felt very faint, went home and was put to bed. For several days he noticed black stools and all symptoms, which had been present three years previous to the operation, returned. Gastro-intestinal X-ray at that time showed a gastroenterostomy functioning well and also some of the meal passing through the pylorus. Doctor Imboden did not find any X-ray evidence of ulcer. With medical treatment and diet there was some improvement but every few weeks the old symptoms recurred. About the middle of November, 1929, he felt pain while sitting in his motor car and vomited a large amount of blood. On November 26, 1929, he entered St. Francis Hospital with hæmoglobin of 30 per cent. and had a transfusion of 600 cubic centimetres of blood by the Unger method. On December 2, 1929, with spinal anæsthesia Doctor Russell resected the distal half of his stomach and duodenum containing the scar of the former ulcer, which had healed, there remaining a minute ulcer from which it was evident that he had been bleeding. The distal end of the stomach was closed and the gastroenterostomy which had been made five years before retained. This operation really amounted to a Billroth II. Careful examination of the resected portion of the stomach revealed numerous areas of ulceration. On the third day after the operation pneumonia developed in the two lower lobes of the right lung and patient was extremely ill for several days. However, he recovered and has been free from all symptoms except a little gas to the present time.

The second patient, a man, fifty-three years of age, was admitted to St. Francis Hospital March 8, 1930. Six years ago had typhoid fever. Four years ago was operated upon by Doctor Russell at the Post-Graduate Hospital for duodenal ulcer. At that time the appendix was removed, a penetrating ulcer was excised and a posterior gastroenterostomy was performed. He had had ulcer symptoms for twelve years prior to this time. He states that he has been symptom-free until the present attack which began three weeks ago, at which time he fainted in the toilet early in the morning immediately after arising. He had no pain but vomited some mucus and passed tarry stools for several days. He was very weak but continued to work. Three days ago he again had a weak spell and began to pass tarry stools

which have continued to the present time. Hæmoglobin at the time of admission was 28 per cent. Appears very pallid and weak.

On March 10 he was given 620 cubic centimetres of blood by the Unger method of transfusion. On March 13 X-ray showed marked deformity of duodenal region. On March 17 a second transfusion of 500 cubic centimetres of blood was given him. Immediately following the transfusion, under spinal anæsthesia, the distal half of the stomach and first portion of the duodenum were excised. There were multiple erosions of the pylorus and duodenum found in the removed specimen. The gastroenterostomy which had been performed four years before was retained and the end of the stomach sutured. The pathologist reported numerous ulcerations about the pylorus and duodenum with areas of superficial hæmorrhages. The patient states that he is now feeling well and eats whatever he wants.

The third case presented was a man, twenty-six years of age, who was admitted to St. Francis Hospital November 3, 1929. At that time he stated that he had been a patient in same hospital for operation upon the stomach early in 1926 and again in autumn of 1927. The records showed that a duodenal ulcer was excised in 1926, and a posterior gastro-enterostomy had been performed in 1927. The chief complaint was pain in the epigastrium, slightly to the left side, one or two hours after meals. Until recently the pains had been relieved for a short while after meals. These pains have been present since leaving the hospital in 1927, but have become worse, especially at night, during the past week. He has frequently noticed that his stools have been very dark. X-ray report of November 8, 1929, shows a filling defect of the duodenum indicative of ulceration. There was also noticed retention of a small amount of barium at a point corresponding to the distal end of the gastroenterostomy opening. Diagnosis of marginal ulcer was made. Under spinal anæsthesia November 15 the abdomen was opened through the former scar and a large ulcer found encircling the distal third of the cloaca. The stomach and intestine were dissociated. The distal two-thirds of the stomach and scarred duodenum were excised. The cut end of the stomach was sutured to the opening in the intestine after the method of Polya. The patient was discharged December 14. He says that he is feeling very well but when seen ten days ago, which was the first time he has seen a doctor since leaving the hospital, he did not look well.

The fourth case presented was a young man, aged nineteen and a half years. He was admitted to St. Francis Hospital January 2, 1930, giving the following history:

Appendix was removed in same hospital two months ago. He still complains of epigastric pain which has not been influenced by the appendectomy. The pain begins two hours after meals and continues until the next mealtime. Pain is relieved by bicarbonate of soda which he has been taking for a long time. He has frequently noticed that his stools have been black. He has vomited frequently during the past few weeks but has not noticed any blood in vomitus. Gastro-intestinal X-ray showed a very large stomach low in the abdomen. The duodenal caput is small and irregular in outline suggesting ulceration. January 10, 1930, with spinal anæsthesia, a penetrating ulcer of the lesser curvature of the stomach was found  $1\frac{1}{2}$  inches to the inner side of the pylorus. The distal two-thirds of the stomach was removed after the method of Polya. A few weeks later this patient returned to the hospital and had his tonsils removed. He said he was then symptom-free.

BLEEDING GASTRIC AND DUODENAL ULCERS. REPORT OF  
FIFTY-TWO CASES

DR. J. WILLIAM HINTON read a paper with the above title for which see page 844.

DR. JOHN F. ERDMANN said if one reviews the varied opinions that have been expressed during the past few years regarding this condition it will be clear that they have changed as often as those of ruptured tubal pregnancy cases. At one time these extrauterine patients were not treated until the bleeding had ceased. Of course, by that time some of the patients had also ceased, and this is the same with ulcer cases. With the advantages of transfusion, etc., of the present day an actively bleeding ulcer is, in the opinion of Doctor Erdmann, a surgical entity, a case for surgical interference. When one is satisfied by physiological examination of the blood, pulse, etc., that the hæmorrhage has ceased, the operative procedure can be delayed. He did not believe that the first hæmorrhage would always result in non-mortality, as had been stated so many times. For that reason, he took the stand that a case with rapidly increasing pulse and increase in the leucocyte count is a patient for active surgical treatment. It is not necessary to discuss the type of operation; it is enough to say that some operation is indicated. Doctor Erdmann wished also to affirm that the patient with recurring hæmorrhage is absolutely a surgical entity. The cause has not been removed if there are repeated hæmorrhages, although by the aid of the X-ray one can note if there is evidence of repair of the ulcer. There are today a number of surgeons and medical men walking about with ulcer of the stomach or duodenum, being watched very carefully by repeated X-ray examinations. If the X-ray shows the ulcer is diminishing the patient can remain under observation; if the ulcer is not diminishing in size or shows tendency to perforating or a dissecting evidence be found the patient immediately becomes a surgical entity. In regard to the frequency of perforations in the months of March and April and in October and November, Doctor Erdmann believed that careful observation on the part of anyone seeing many of these ulcer cases, will show that the greatest activity occurs in the spring and fall months. Certainly, in Doctor Erdmann's office, just as soon as a patient stated that he felt worse in the spring, or in the fall, it was felt that he had an active gastric or duodenal ulcer to contend with. In contemplating the figures of fifteen patients, with four deaths, in unoperated cases, and twenty-seven operations, with 16 per cent. mortality, one is driven to believe that the only thing to do is to consider the condition of the patient as he presents himself in the hospital. Every such patient has been bleeding for some time, and it is quite possible that there will be a cessation of the hæmorrhage at the time of admission. It is, therefore, not fair to estimate the patient's condition when he is first seen. Under observation it will be noted whether or not the hæmorrhage is persisting.



DR. FREDERIC W. BANCROFT said that he was very much interested at the present moment in the problem of six patients with bleeding who had died without operative interference. The speaker had held several discussions with physicians who declared they had never seen a patient die from gastric or duodenal hæmorrhage as such. He wished to ask Doctor Hinton what proof he had that his cases were solely duodenal or gastric ulcers and what diagnostic means were used.

DR. WILLIAM CRAWFORD WHITE inquired as to immediate operative interference in the acute cases, to what extent one should go in making a diagnosis of bleeding from an ulcer as such. It had been his unfortunate experience to operate on cases which were thought to be bleeding ulcer, but careful investigation failed to reveal any ulcer. To what extent should one go forward in such cases? If one waited for X-ray examinations and other data one then began to deal with a chronic case and by that time the chances were that the patient was recovering. It appears from the paper of the evening that the cases that died from hæmorrhage are those that have an overwhelming hæmorrhage with death shortly after the onset.

DR. KIRBY DWIGHT said that for years he had not been operating on these cases of bleeding from the stomach or duodenum unless there was indication for it after the hæmorrhage had stopped, and therefore had not had much opportunity to note the pathology of the stomach at the time of bleeding, but he remembered that as an interne under Doctor Blake these cases were operated on while actively bleeding and several that showed no pathology by palpation of the stomach, no induration, no crater, on opening revealed numerous small erosions, with no definite ulcer and no definite bleeding points that could be ligated.

DR. HERMANN FISCHER said that active interference in cases of acute hæmorrhage was open to question and still a mooted point among surgeons. A correct diagnosis of the origin of the vomited blood is sometimes very difficult to make and the decision, whether one has to deal with hæmorrhage from the duodenum or stomach, or hæmorrhage of a different origin, becomes of the greatest importance. He had seen patients with severe bleeding in whom the diagnosis of gastric ulcer was made and in whom at operation no ulcer could be found. Several had multiple erosions so-called Reichmann's disease and some œsophageal hæmorrhage, and some hæmorrhage from the bowels secondary to venous congestion in the portal system. All these factors made him inclined to temporize. He had been rushed into operations which had proved without benefit; on the other hand, he had seen patients *in extremis* recuperate from the hæmorrhage and remain perfectly well, although in such cases he believed the hæmorrhage was caused by other pathology than ulcer. Doctor Fischer wished to accentuate the importance of making a diagnosis of the origin of the hæmorrhage, which is not so easy, especially in an emergency.

## BLEEDING GASTRIC AND DUODENAL ULCERS

DR. DEWITT STETTEN said there has been a long-standing superstition among gastroenterologists that from a bleeding ulcer death never occurs and Doctor Stetten has heard this view stoutly maintained by some of the leading gastroenterologists of the country. The speaker has personally seen at least three such deaths confirmed by autopsy. In these cases there were large infiltrated ulcers on the lesser curvature or posterior wall of the stomach and in two of them a large patent artery could be seen at the base of the ulcer. The myth that death cannot occur directly from a gastric hæmorrhage due to a bleeding ulcer should be permanently exploded, because such deaths certainly do occur and are not so very uncommon.

DR. FRANK S. MATHEWS said that some years ago he encountered two ulcers while they were bleeding and, finding the general condition good, did a transfusion and immediate operation. The result was conspicuously successful. Encouraged by these cases, he followed the same technic of transfusion and operation in a case of fairly severe hæmorrhage. At the operation a long search through the upper abdomen failed to reveal the source of bleeding. In this patient, the bleeding has not recurred in over three years. He was more cautious in the next case. He treated the patient medically until health was restored. One year later the patient had another hæmorrhage. At operation, three weeks after the hæmorrhage, the pylorus was incised and no point of bleeding could be located. In the past year this patient's bleeding has not recurred. He wondered whether the bleeding point might not at times be from a fairly superficial ulceration even though the quantity of bleeding was considerable; and whether such a bleeding surface might not heal over in a fairly short time. In another case of gastric hæmorrhage, an incision into the body of the stomach revealed the point of bleeding in what looked like a fissure quite close to the greater curvature—a part of the stomach where one would not expect to find an indurated ulcer. He believes no single rule can be laid down to guide one in the selection of treatment in such cases.

DR. RICHARD LEWISOHN said that he did not agree with Doctor Hinton's statement that "it is very questionable whether partial gastrectomies are ever indicated in bleeding lesions, either of the stomach or duodenum." There can be no question that medical treatment of bleeding duodenal ulcer is followed by a considerable mortality. On the other hand, it cannot be denied that surgical intervention is not devoid of danger. Simple gastroenterostomy is not apt to cure a bleeding ulcer, and if any operation is performed partial or subtotal gastrectomy must be resorted to. The majority of bleeding ulcers are located on the posterior surface of the duodenum near the pylorus. Therefore, local excision is impossible in most of these cases. An attempt should be made in cases of duodenal ulcer to remove the ulcer. When dealing with a duodenal and gastrojejunal ulcer at the same time, and when the condition of the patient warrants it, it may be advisable to perform the Finsterer type of resection, a method that insures

a complete sidetracking of the food and a marked reduction in gastric acidity and thus facilitates healing of the ulcer of the duodenum. Conservative treatment should be attempted first in every case of acute bleeding ulcer. When the symptoms persist, however, surgery in the form of gastric resection must be resorted to in order to save the life of the patient, even in the presence of severe anæmia.

DOCTOR HINTON, in closing the discussion, said that autopsies were performed on all the cases that died under conservative treatment. In the cases of hæmatemesis and tarry stools the diagnosis of ulcer had been made either by X-ray, operation or autopsy, or from the previous history and treatment. If all the cases of gastro-intestinal hæmorrhage had been included in this series there would, in all probability, have been between 125 to 140 cases instead of the 52 cases reported. As to what method of treatment should be followed in cases of bleeding ulcer was difficult to decide, particularly when reviewing some of the cases reported that evening. One case, operated upon eighteen years ago, at which time gastroenterostomy had been done, was symptom-free from 1910 to 1928 and then had a profuse hæmorrhage. Another patient was treated for an ulcer and was symptom-free for twenty-five years and then had a gastric hæmorrhage. A third case first had a pyloroplasty for a bleeding ulcer and two years later a partial gastrectomy for pain, and two years after the second operation had a profuse hæmorrhage. Doctor Hinton said that his reason for stating that a partial gastrectomy seems very questionable in cases of bleeding ulcer was the information he had received within the past ten days that in Rochester, Minnesota, during the present year they have operated upon five cases of marginal ulcer following subtotal gastrectomy, all of these cases having originally been operated upon by the same surgeon in New York City.

## BRIEF COMMUNICATIONS

### MAGGOTS IN THE TREATMENT OF INFECTED WOUNDS, COMPLICATED FRACTURES, OSTEOMYELITIS AND TUBERCULOUS ABSCESSSES

SINCE William S. Baer, of Johns Hopkins University, has revived in America the use of maggots (since 1928-1929) in the treatment of osteomyelitis, Kleinberg, of the Hospital for Joint Diseases, New York; Rechtman, of Philadelphia; Taylor, of Coatesville, Pa.; and others have been using this ancient remedy.

Cattell, editor of the International Clinics (Philadelphia), informs me he called attention to the unusually clean condition of battle wounds in France (1918) that were infested with live maggots. He discussed this interesting observation with men of Base Hospital No. 2.

D. P. Murphy, of Philadelphia, informs me (personal communication) that a friend told him that in 1866, a German doctor kept small tin boxes of maggots on his shelf. He put a box-full of live maggots in an infected wound of his hand and fingers (the result of an infected black spider-bite) and gave him (the patient) an equal amount of maggots to be used for redressing at bedtime. Fresh maggots were put in twice daily for ten days—using only dry gauze. The patient says it saved his fingers—which other surgeons had wished to remove. Since the German doctor was old then—in 1866—he must have been informed of Baron Larrey's work in the Napoleonic Wars. This patient, now eighty-four years of age, remembers the details most vividly. He recalls his doctor was very old and had palsy.

I will quote translating from Larrey's *Clinique Chirurgicale*, Paris, vol. i, pp. 51-52, 1829: "There is still a particular form of foreign body which should be considered. This form was observed by the author in most of the wounded soldiers in Syria during the Egyptian expedition. During suppuration of wounds, these wounded soldiers were inconvenienced by *larvæ of the blue fly*, common in that climate. These insects formed in several hours, developing with such a rapidity that in one or two days they were the size of a small quill. This greatly frightened the soldiers in spite of all efforts to reassure them. It was only after experience that they could be convinced that, far from being injurious to their wounds, *these insects accelerated cicatrization by shortening the work of nature and by producing an elimination of the necrotic cells by devouring them*. In fact, these *larvæ* only consumed putrid material and did not disturb any living tissues. No hæmorrhages were ever observed under these circumstances regardless of the depth to which the insects penetrated or the extent of the wound. Lotions consisting of a strong decoction of garlic, rue or sage applied at each dressing

sufficed to destroy them but they returned soon afterward on account of the lack of means for preventing the approach of flies or preventing incubation of the eggs. This can be accomplished by moistening the first compress in a solution of camphor or some other antiseptic fluid."

I have found no direct references to the use of maggots in the works of Guy de Chauliac (1340-1365), Henry de Mondeville (1330-1360) nor in Ed. Nicaise's Editions of Chauliac's and Mondeville's works (Paris). Some of the works of the following authors may contain such references but I have been unable to locate them: Ambroise Paré (1510-1590), Delacroix, Fallopius, Magatus, von Bilguer (1763), Paul of Aegina (7th Cent.), Rogerius (13th Cent.), Bouve (13th Cent.), De Vigo, Paracelsus, Vesalius (1514-1564), Le Dran (1730), Rivinus (1652-1723), Benjamin Bell (1749-1806), Astley Cooper, Heister, Percy, Lombard, Goulard, Sampson Gamgee, Richard Wiseman, and Pierre Franco (1561). Malgaigne (1847) does mention the value of maggots and quotes Larrey's observations. Packard in his translation, of course, mentions it (1859).

In "Selections from the Works of Ambrose Paré," by Dorothea Waley Singer, I find on page 84, line 18, under "Gunshot Wounds": "If any (wounds) chanced to bee undrest for one day—the next day the wounds would be full of wormes."

Jas. Henry Breasted's (1930) work on the Edwin Smith Surgical *Papyrus*, vols. i and ii (London, Cambridge University Press) makes no reference to maggots. Agnew's Surgery, vol. i, page 254, second edition, 1889 (Lippincott, Philadelphia) refers to maggots in wounds and how best to treat them.

I do not doubt but that the old Egyptian, Hindu, Indian and Arabian surgeons may have known of the value of maggots in the treatment of infected wounds and bone infections—but exact references are not available to me. It would be of interest from a historical standpoint to make a careful search of the ancient medical writings. I do not know of any Talmudic references to this subject.

W. W. Keen, of Philadelphia, says: "During the Civil War maggots were very common in the summer—the resulting maggots were certainly disgusting, but, so far as I ever observed, they did no harm." Crile (1917) says that, on the contrary, they actually do good. This would probably be especially true in cases of infection from the bacillus of gas gangrene.

Geo. W. Crile, speaking before the Clinical Congress of Surgeons of North America, "War Session," October 23, 1917, said: "In the wounded who lie out in 'No Man's Land' for two or five or ten days, it has been found that the wounds that have done best are those that contain maggots. The reason for this is that there is devitalised tissue; the maggots live on this devitalised tissue, and if they destroy that tissue they do in time what the surgical operation does."

Dr. Edward Martin, of Philadelphia, said (October 23, 1917) before the same session of the Clinical Congress of Surgeons of North America: "They

had been advised by one eminent member of the profession to take all the antiseptics and throw them into the sea, and another had advised them to raise a brood of tame *maggots to take care of the wounds.*"

In August, 1929, on a visit to the Provincial General Hospital of Madrid, Spain, I saw maggots being used in treatment.

There is a short article on this subject in *Science*, Supplement, p. 12, November 29, 1929.

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## THE UTILIZATION OF TWO OPERATORS WORKING SIMULTANEOUSLY ON THE SAME PATIENT

It is now a well-recognized fact that excessive speed in the performance of surgical operations is no longer the indication of the best surgery, but that moderate speed with greater consideration for tissues and attention to detail is much more desirable. Of course any manœuvre which will cut down the time of an operation and consequent length of anæsthesia is advantageous, so long as it does not interfere with careful work. The purpose of this note is to call attention to a plan which we have been using with a great deal of satisfaction and which doubtless others also use, or could use.

The reason for calling attention to this matter is that visitors observing our routine have remarked that the use of two operators working at the same time on the same patient was out of the ordinary. In general plastic surgery, we are constantly dealing with patients on whom two operative procedures may be carried out simultaneously on different portions of the body, and this may also be done in suitable cases in general and in orthopaedic surgery.

For instance while one operator with his team is preparing an area to be skin grafted, the other can be cutting the Ollier-Thiersch, or whole thickness graft; while a part such as the hand is being made ready by one operator, a flap either for immediate transfer, or following a delayed transfer, can be prepared by the other.

Where fascia, or fat and fascia, or costal cartilage, or bone transplants are to be used, the areas into which they are to be transplanted can be prepared by one surgeon while the graft is being obtained by the other, etc., etc.

It is essential for the successful use of two operators that a competent and experienced associate be available who is familiar with the methods and needs of the surgeon in charge, and, of course, two operating teams are necessary.

I remember very well the first time the simultaneous use of two operators came to my attention. Many years ago while I was resident surgeon at the Union Memorial Hospital, a patient was admitted in Doctor Finney's service with bilateral gangrene of the feet. His condition was critical and immediate amputations were imperative, so in order to save time, Doctor

Finney asked me to remove one foot while he amputated the other. From this incident, with its evident advantage to the patient, developed the regular use of the method in my work.

Where two operative procedures which may be done at the same time on different parts of the body are necessary in order to accomplish the desired result, they should be done simultaneously.

For a number of years I have planned in advance for two operators and two teams on all cases where conditions are favorable and find it a great saving in operating time and much to the benefit of the patient. The procedure is particularly helpful in reconstructive work.

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### CYSTIC MYOMA OF THE BROAD LIGAMENT

INTRALIGAMENTOUS cystic myomata are uncommon. Kelly and Cullen in their authoritative dissertation on uterine myomata state that in 1,600 of



FIG. 1.—Intraligamentous cystic myoma. External view.

their own cases of myomata they did not encounter any such type of growth. The records of Charity Hospital of New Orleans for the past twenty-four years fail to reveal the occurrence of any intraligamentous type of myomata.

## CYSTIC MYOMA OF THE BROAD LIGAMENT

Our search of the literature reveals only six such cases reported. This has prompted presentation of the present case.

**CASE HISTORY.**—Mrs. B. S., white housewife, age forty, was admitted complaining of pain in the lower abdominal segment for the previous eight months. The pain was dull in character and seemed more severe in the right lower quadrant than in the left. The past history revealed that an appendectomy had been performed fourteen years ago, but nothing of importance. *Physical Examination.*—Reveals nothing remarkable except a lipoma about the size of a small orange in the lumbar region on the left side, and tenderness in the lower portion of the abdomen. Vaginal examination reveals a hard mass to the right of the normal position of the uterus. This mass is tender and seemingly movable with the uterus.

Under gas anaesthesia, a mid-line incision was made between the umbilicus and the pubis. The intestines and omentum were packed upward with large gauze packs. The

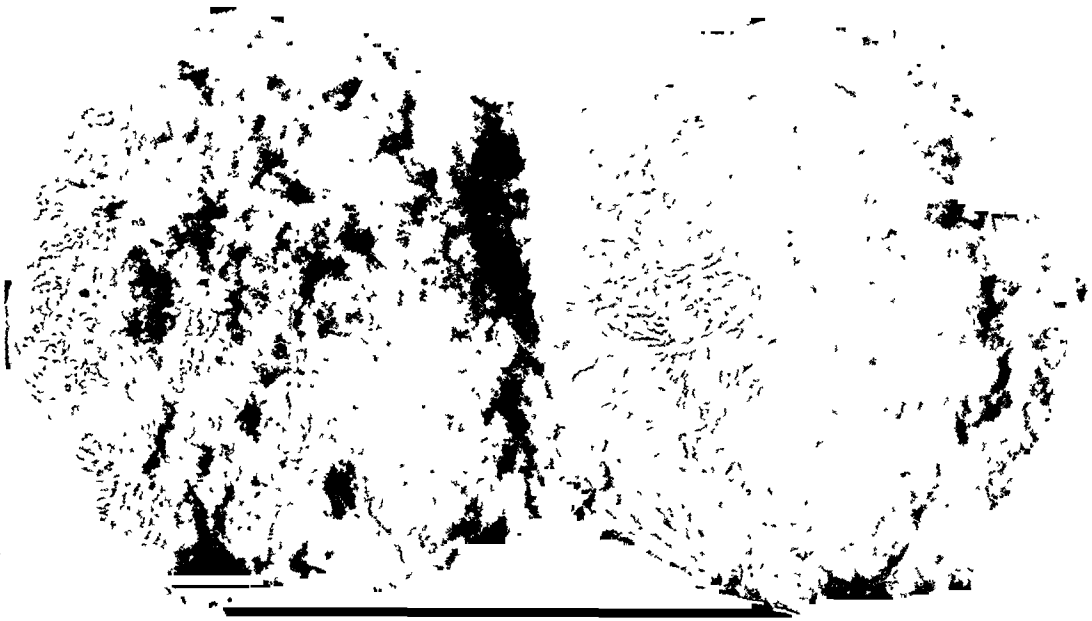


FIG. 2.—Intraligamentous cystic myoma surfaces revealed by sectioning.

uterus was found to be small, its right lateral aspect over-riding a tumor slightly oblong in shape, nodular, about the size of a large orange, and situated within the folds of the right broad ligament. A pedicle carrying two or three small blood-vessels apparently was the only connection existing between the tumor and the myometrium. The folds of the broad ligament were incised and the tumor mass enucleated. During this enucleation, there was hardly any bleeding as practically all of the blood supply came from the vessels entering through the pedicle. The pedicle was clamped, severed from the tumor mass and ligated with chromic No. 2 catgut. The folds of the broad ligament were closed with chromic No. 1 catgut. There being no bleeding and the appendix having been removed at a previous operation, the packs were removed and the incision closed in the usual manner by layers.

*Gross Observation of Removed Tumor.*—The specimen consists of a mass of tissue generally rounded in shape (Fig. 1), measuring 9.5 by 7.25 by 6 centimetres. Externally, the tumor is markedly nodular, grayish-pink in color and devoid of peritoneum. At one point there appears a small pedicle containing three or four small blood-vessels with a plexiform arrangement of these vessels at their point of entry and exit in the tumor. Here and there small cysts can be noted beneath the surface. Surfaces presented by sectioning (Fig. 2) reveal a pinkish-gray color with a whorl-like arrangement of



myomatous tissue, the tumor being markedly lobulated with cysts varying in size from a few millimetres to 0.5 centimetre in diameter occurring throughout. The cysts contain clear, straw-colored, mucoid material.

*Discussion.*—The intraligamentous myomata previously reported all occurred on the left side. Eden, A. J. Smith, and Langley found only a few strands of tissue existing between the tumor mass and the uterus. In Janicot's and A. L. Smith's cases, distinct connection between the myomatous tumor and the uterus could be demonstrated. All of the growths were within the folds of the broad ligament and were readily removed. In Langley's case, it was necessary to dissect out the left ureter in order to properly control all bleeding. In addition, this case showed a small subperitoneal myoma on the posterior uterine wall. In A. J. Smith's, A. L. Smith's and Rosenberg's cases, the tumors had caused dissection of the posterior peritoneal covering of the uterus into the broad ligaments of the opposite side.

The gross and microscopic structural similarity of the various tumors is marked. They consisted of masses of myomatous and fibrous tissue with interspersed multiple cysts, some being microscopic in size, others rather large. Retrograde changes were prominent. Janicot alone found epithelium lining in the cyst-like cavities, one such cavity in the body of the tumor being so lined. In all cases some connection, even though at times slight, could be noted between the uterine body and the tumor. We subscribe to the belief that such growths spring from the uterine body and not from the smooth muscle fibres normally present in the broad ligament as believed by Eden and A. J. Smith.

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TUBERCULOSIS OF THE DUODENUM, LIMITED TO  
THE PAPILLA OF VATER\*

TUBERCULOSIS of the duodenum seems to be even more uncommon than that of the stomach. In 5,900 autopsies, including 2,360 with evidences of tuberculosis elsewhere, Goosman found it but five times, either alone or as part of a general intestinal involvement. The reason for this rarity is not clear, although it has been thought to be connected with the antiseptic properties of the gastric, pancreatic and biliary secretions. The bile, however, may perhaps be excluded by the fact that the tuberculous ulcer in the case here reported was situated around the opening of the common bile duct—apparently a unique observation. It also is interesting to note that the trouble has been found where there was little if any acid in the stomach. Clinically only six cases have been reported according to Röpke,<sup>1</sup> four in men and two in women, two of these being over fifty years of age.

The most likely source of infection is thought to be by way of the stomach, possibly upon the basis of an old duodenal ulcer, although consideration must be given to the blood-vessels and the lymphatics, especially those connected with diseased retroperitoneal glands. In the case here reported a tuberculous lymph node was found, but it was the only one and seemed obviously secondary to the duodenal ulceration. In nearly all instances the duodenal lesion has been secondary to tuberculosis elsewhere, although Höfer has reported one that was primary and my own case appears to be of that nature. The ulcers nearly always are situated in the proximal portion of the duodenum, but they may appear elsewhere.

There seems to be little that is characteristic about the symptoms, which may, indeed, resemble closely those of ordinary ulcer. There is frequently, however, a tendency to stenosis, which, in connection with diarrhoea and the manifestations of ulcer may, according to Röpke, arouse suspicions of tuberculosis; but an exact diagnosis is difficult if not impossible. In spite of its rarity, however, the possibility of tuberculosis should be borne in mind in gastroenterostomies for ulcer of the duodenum, especially when the ulcer refuses to heal.

The treatment suggested by Röpke is resection of the affected portion of the duodenum when practicable (three cases reported), followed by the use of the X-ray and heliotherapy. These latter measures, however, would seem to be uncalled for if the operation has been a thorough one, the excision of the ulcer alone, together with infected lymph nodes, perhaps being sufficient, as in the instance under consideration.

CASE REPORT.—The patient was a thin, moderately jaundiced woman, fifty-two years of age, without pain, tenderness or attacks of colic, who had lost about 100 pounds in weight. The jaundice had existed for two years, and was subject to irregular variations in intensity. There were indefinite stomach symptoms, with a tendency to nausea, and vomiting an hour or so after meals. Some sixteen months previously a cholecystectomy had been done, but no improvement resulted except relief from a certain amount of pain.

\* Read before the Western Surgical Association, December 5, 1930.

The stools were clay-colored. No blood had been vomited or passed by the bowel. Since this operation, she has had frequent attacks of persistent diarrhœa. One sister had suffered with pulmonary tuberculosis, but there was no history of the trouble in the remainder of the family or in herself, and no signs of pulmonary or other tuberculous foci could be detected. Bleeding time  $2\frac{1}{2}$  minutes; clotting time 5 minutes; hæmoglobin 70 per cent. An X-ray examination was negative, including the stomach.

At an exploratory operation done September 2, 1929, under a diagnosis of obstructing stone or tumor, a greatly dilated common duct was found. The liver was swollen and congested, with rounded edges, but there was nothing abnormal about the stomach or pancreas and no tumor was detected. Exploration of the duct revealed an impassable stricture at its orifice, but no stone. The duodenum was then opened with a transverse incision and an ulcer exposed surrounding the papilla of Vater. It was about the size of a little finger nail, somewhat raised above the surface, almost like a sessile papilloma, and was soft and vascular, with the opening of the bile duct in its centre. There were no other lesions of the mucosa. Exactly in the angle between the common duct and the duodenum, and in intimate relation with the ulcer, was a solitary caseous lymph node the size of a small olive, which may have contributed to the biliary obstruction.

The ulcer was excised, together with small terminal portions of the common and pancreatic ducts, the openings of which were then stitched to the surrounding mucous membrane. After removal of the caseous gland, a choledochoduodenostomy was done in order to insure a free outflow of bile if a stricture should form. The incisions in the duodenum and common duct were then closed, the suture lines covered with omental tags, and a temporary drainage tube inserted in the foramen of Winslow, which was removed in four or five days. There was no leakage of bile and the convalescence was uneventful, except for a rather troublesome post-operative diarrhœa lasting for a week or so. The jaundice existing at the time of operation soon disappeared and the return of health and strength was rapid, the patient reporting, some eleven months later, that she had gained enormously in weight and felt perfectly well. The laboratory report on the specimens removed was tuberculosis of both lymph node and ulcer.

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<sup>1</sup> Röpke: Beitrag zur Klinik der Tuberculose des Zwölffingerdarmes und der Magen.  
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## CORRIGENDA

In the January number, p. 430, 23d line from top, for the figures "160" substitute "60"; p. 431, 15th line from top, for "figure 5" substitute "5%"; p. 434, 9th line from bottom, insert word "with" after word "while," so as to read "while with others, etc."

## EDITORIAL ADDRESS

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# ANNALS *of* SURGERY

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## DELAYED AND NON-UNION IN FRACTURES IN THE ADULT\*

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THE results of trauma occupy a unique position among surgical conditions in this age of economic urge, since they frequently are directly traceable to the patient's occupation and result in temporary or permanent disability. A generation ago this mattered but little to anyone except the individual involved—he was essentially responsible for his own medical care—his was the worry as to time lost, doctors' bills, and eventual outcome.

With the universal enactment of some form of workmen's compensation legislation, these problems with their financial burden have been shifted from the individual to the employer and his insurance medium—they have become business problems.

With this shift in responsibility has come the realization of the tremendous economic loss through injury each year, and with that realization has come a demand upon the profession from organized industry for a shortening of convalescence or disability time and a diminished percentage of permanent disabilities and, by these means, a reduction in treatment costs.

One of the frequent factors with which we have to deal in meeting these demands is delayed union and non-union in fractures. I say frequent, because I use the term "delayed union" in the sense of prolonged healing time. It will, therefore, include many fractures which heal in what is called the normal or average time for the region involved, where that time is an extended period.

I feel that the problem presented to us by delayed and non-union is primarily not one of how to treat these conditions, but rather of how to prevent their occurrence and how to reduce the time required for healing in those regions where it is expected that normal or average healing time will be prolonged. I might point out the fact that to industry and to the patient the time taken to secure a given result may be just as important an economic factor as is the result obtained. In the satisfied contemplation of end-results we are apt to overlook this aspect of the case. It is equally true that, in general, our efforts to maintain adequate bony anatomy during a prolonged healing time are reflected in functional inactivity of the part as a whole, with consequent soft-part disturbances from which it may take the patient considerable time to recover. Hence the so-called "after-treatment" of fractures. We are dealing essentially with a healing process of dual nature. A wound

\* Read before the New York Surgical Society, April 8, 1931.

of bone must heal, and the healing tissue must be fortified by deposited calcium to constitute a rigid fusion of the wound margins. In experimental work presented at the Scientific Exhibits of the American Medical Association in 1927, 1928 and 1929,<sup>1</sup> I adduced adequate evidence of the fact that all fractures heal unless there exists a physical or chemical bar to the growth of granulation tissue, and that the healing process is, as with any other wound, the result of granulation tissue growth. The physical bar may exist as interposed tissue or massive death of tissue in the fracture region. The chemical bar may be infection or any other chemical agent which destroys fibrin or growing cells.

The terms delayed union and non-union as commonly used refer to delay in or failure of the process of calcium deposition in this healing tissue to form bone. To logically treat or prevent delayed or non-union we must, therefore, understand what happens during this process.

*Although today there exists, to say the least, serious doubt as to the existence in the adult human of a specific bone-forming cell—an osteoblast—it is commonly assumed that the healing of a fracture occurs through an actual growth of bone from the site of fracture.* I do not believe this to be true, and in a previously published article<sup>2</sup> I have shown that as much as 60 per cent. of the healing tissue which is subsequently calcified may be derived from tissues outside the bone in muscle and fascial planes and that any tissue not so derived comes from the *soft parts of the bone*—the so-called endosteum, the periosteum and the areolar tissue about the blood-vessels.

I presented evidence at the same time supporting the view that this living tissue was calcified without the activity of any specific cell and that the calcium utilized was derived from the demonstrably dead bone ends at the fracture site through obvious autolysis, and not from the blood-stream calcium which is the source of the calcium used in the ordinary growth structural changes in bone; and that in experimental animals as much as 2.5 centimetres of bone with its periosteum could be removed and the gap allowed to heal in the presence of an artificially supplied calcium source placed therein with a resultant solid bony union of the gap.

In another paper<sup>3</sup> I cited the evidence to support the view that bone can be formed anywhere in the adult body if four requisite conditions are fulfilled. They are: 1, Death of tissue; 2, granulation tissue growth; 3, a local concentration of calcium to act as a calcium source; 4, a proper pH of the tissue fluids in the specific region involved, which is, in part, dependent upon the lymphatic and vascular circulatory status of the part from both a qualitative and quantitative viewpoint. On the basis of this conception I was able to demonstrate in 1930<sup>4</sup> the production of experimental myositis ossificans with true bone formation without the introduction in the muscle of any bone elements whatever.

Going a step further, utilizing tissue culture as a medium of investigation, I have presented evidence to show that the morphological counterpart of new bone can be produced in a plasma medium in the total absence of cells by

purely biochemical means—artificially creating the factors which I have cited as essential for new bone formation—and have produced evidence to support the viewpoint that the enzyme phosphatase, which is held by many as responsible in the mechanism of depositing calcium in the tissues to form bone, is liberated by the death of cells rather than as a product of their living metabolism.<sup>5</sup>

The amount of callus produced in any given fracture, and the rapidity of its production and increasing density, would appear in the light of the above data to depend upon the mechanical factors cited, the possible sources for granulation tissue growth and its unimpeded progress, the rate of autolysis of dead bone at the fracture site (influenced by tissue fluid pH at that site and the density of the bone to be autolyzed) to give available calcium for deposition in the granulation tissue, and the proper mechanism of deposition involving the question of enzyme activity and the proper pH of tissue fluids for that activity. It would then appear to be a purely local process, independent of factors outside the affected area.

This agrees with clinical facts. Delayed union and non-union are, if we exclude the cases in which actual healing is prevented by the mechanical or chemical factors cited, phenomena of certain locations in the body and not of individual patients, if reasonably proper treatment methods are used. The evidence on this point is overwhelming. The patient with a fracture of the intertrochanteric region of the femur—regardless of age, general health, specific disease or blood chemistry—heals by bony union so universally that it is jocularly said that he heals despite the treatment accorded. In the patient with a fracture two inches away—in the so-called intracapsular portion of the neck—we look forward at best to a slow formation of scanty callus, and we expect a large percentage risk of non-union or even bone absorption. And in this group of neck fractures we have no criterion whereby we can say what is going to happen in any given patient. We have carefully observed our patients from this standpoint. We have seen a patient of twenty-eight in perfect health go on to a non-union, while an octogenarian dying at nine weeks from intercurrent disease showed at autopsy a solid bony healing under identical treatment methods. A woman of forty-eight under ideal conditions had extensive absorption of the neck at eight weeks, while a coincident case in a senile woman of seventy-three, who had a hemiplegia a few days after her spica was applied and then developed a pyonephrosis with a daily temperature of  $103^{\circ}$  to  $105^{\circ}$  for the next six weeks, during which time she was in coma and completely involuntary, at eight weeks had evidence of bony healing and is today walking about on a perfectly good femoral neck.

What difference exists between the neck of the femur and the intertrochanteric region? The neck is surrounded by the dense fibrous reflection of the capsule of the joint. When it is broken it has only its own meagre soft parts and this dense fibrous tissue as a source for granulation tissue healing. It, therefore, never shows much callus. Its blood supply is minimal to begin with. Depending upon the damage inflicted by the original injury,

or that subsequently allowed or inflicted by improper treatment, this is cut down to a varying degree, and may be qualitatively changed as well. The calcium which is demonstrably autolyzed from the obvious dead bone at the fracture site cannot be utilized because of tissue pH conditions. There is an additional factor—the presence of synovial fluid. Cells cannot grow in a fluid medium with any degree of success and so tissue growth is hindered. Synovial fluid acts not as a deterrent to *bone* growth, but to *any* growth. This condition may well be reflected in other regions in the presence of marked œdema of the part.

The intertrochanteric region is buried in large vascular muscle bellies which surround the fracture site on every aspect. They are an adequate source for profuse granulation tissue growth and provide tremendous accessory circulation to make up for the damage done by trauma. The calcium autolyzed from the dead bone at the fracture site is readily made use of and so we see a large mass of callus, rapidly calcified, as a characteristic of the healing process.

Fractures at the junction of the middle and lower thirds of the tibia are characteristically slow in union and frequently show non-union. They are in that region where the inner aspect of the bone is covered by skin only and where the other two faces are covered principally by tendinous structures or narrowing muscle bellies at their junction with tendons. The area of muscle attachments is higher up. So is the region for rapid healing time. Moreover, if one observes the healing process in this region, one will note with marked regularity the formation of callus almost altogether on the outer and posterior faces of the bones, and to a minimal degree on the bare inner face. I desire to call particular attention to the fact that the circulation of the bone itself, as represented by the nutrient vessel, is apparently *not the important factor. It is the accessory circulation available from the soft parts, whether it come via the periosteum, or directly from torn soft parts without periosteal intervention.* Moreover, this circulatory factor plays its part primarily in its effect on the biochemistry of tissue fluids rather than on the nutrition of the part. This same story holds true in those other regions where we may expect slow union and fear non-union—the junction of the middle and lower thirds of the humerus, the scaphoid of the carpus, the head of the radius, the junction of lower and middle thirds of the forearm and the other typical regions.

Mechanical and chemical causes excluded, delayed union and non-union occur in places, not in people.

The viewpoint as to the source of the calcium utilized presented here is borne out clinically. An osteomalacia will heal fractures normally. There is one at our hospital now who, at a time when she had a blood calcium of 6 and a blood phosphorus of 1.2 and was actually running a negative balance, healed a fractured femur in five weeks.

A fragilitas ossium fractures with ease, but heals normally. So does a rachitic, as does a Paget's.

Again, there has yet to be shown any definite benefit from the administra-

## DELAYED UNION IN FRACTURES

tion of any form of medication or treatment affecting the general body chemistry in delayed and non-unions. In my own experience, calcium in every conceivable form by mouth and by injection, cod-liver oil, irradiated Ergosterol, general light irradiation—none has produced any perceptible effect in preventing or curing delayed or non-union.

What, then, are we to do to prevent delayed union and non-union? I shall list below the objects of our concern.

1. Early and accurate replacement of displaced fragments, with assurance at the time of reduction that no interposition of tissue exists.

2. The restoration to normal of lymph and vascular circulation as rapidly as possible through elevation of the part and *early* physiotherapy, and the use of functional muscular activity.

This means bed treatment in the early stage of lower extremity fractures and in many upper extremity fractures. It means the more extensive use of traction-suspension as a method of treatment, particularly of skeletal traction with early active function in traction. It means the application of physiotherapy in the form of heat and light stroking massage starting as nearly coincident with the reduction as possible. It means the augmenting of, and substituting for, normal muscle activity by the use of electrical muscle stimulation to produce a spasmodic contraction of a rhythmical type. This can be secured by the use of a sinusoidal current, by a Bristow coil or by a Smart coil in that order of efficiency.

3. The meticulous care of compounding wounds. Gentleness and conservation of sound tissue are not incompatible with thorough and efficient débridement. For the wound treatment I prefer to use a Carrel technic, but employ an inert solution such as saline, since I am convinced that Dakin's as commonly employed actually removes calcium from the fracture site. I am also quite sure that it pays to be conservative on the score of considering a débrided wound safe to sew up tightly.

Where facilities for operative work on bone are of high standard as regards equipment, technic and personnel, I feel that in open fractures rigid fixation of the fragments by plate or screw at the time of the débridement, with the wound left wide open, is justified by a saving in time through minimizing the chances for delayed or non-union by eliminating the foothold for infection engendered by constant movement of the fragments.

Such a procedure is never justified unless the facilities for carrying it out are as specified.

4. Where the facilities for operative work on bone are of the highest standard as regards equipment, technic and personnel, I believe that open operative reduction is indicated for all fractures with displacement in those regions where prolonged healing time is characteristic, provided there are no contraindications to operation in the particular case involved. I believe that such operative reduction should embody a dual procedure, aimed at the threat of delayed or non-union and malposition as well—following reduction osteo-periosteal grafts or chip should be placed and the fragments fixed rigidly



enough, if possible, so that early active function of the part can be started. The operative approach in proper hands provides the accessory source for granulation tissue and circulatory aid which is so essential to sound healing.

How are we to treat non-union? By creating the essential factors for new bone formation at the site of fracture—death of tissue, adequate granulation tissue—a local source of calcium and an adequate circulatory status for the part—not for the bone alone.

A bone graft, I have every reason to believe, does not grow, but acts as a calcium source for the calcification of the healing granulation tissue, and as one of the sources for the enzymes concerned in the calcium deposition. The removal of fibrous tissue and of sclerotic bone aids circulatory augmentation and granulation tissue growth and invasion. The graft is not efficient enough fixation to allow of early active function, particularly since osteoperiosteal or chip grafts should be the most effective type, and are so clinically and experimentally. I believe that, if possible, there should be added to the graft the rigid fixation obtainable from plate or screw, where it is feasible, followed by early active function. The post-operative treatment of the case should follow the lines laid down for the prevention of delayed and non-union in fresh fractures.

In this connection, and bearing out with gratifying success up to the present the conception of the factors involved in bone healing which have been put forward in this paper, I have presented before this Society two of a recent series of six cases in the characteristic tibial site of delayed or non-union—varying in time from seven weeks to nine months, four of them accompanied by low-grade chronic osteomyelitis due to compounding. Bony union has been secured in all cases within five to nine weeks by the following procedure:—the site of fracture has been widely exposed and the scar tissue from the soft parts removed. A saucerization of the bone in the fracture region back to the posterior cortex has been done. The extent of this has been gauged by the process present. The whole width and most of the depth of the tibia have been removed in each instance, and the extent of sclerotic or infected bone has gauged the length of the removed area. It has varied from 4 to about 7 inches. In some the wound has then simply been packed open with vaseline gauze, a plaster casing applied, and the part left undisturbed for three to four weeks. At the end of that time the packing has been removed and a new jacket applied. The cases so treated showed bony union, but with a greater or lesser saucer-like depression in the front of the tibia, depending upon the amount of bone removed. In other words, they healed by bone, but were deficient in amount. What we had done was simply to kill tissue, to kill some bone by our trauma, thereby supplying a calcium source, and to provide adequate granulation tissue access to the site and adequate circulation by our removal of scar tissue and sclerotic bone and by packing the wound open. Incidentally where infected bone was present, the element of infection had been removed. Qualitatively we had secured our result, but we had actually

removed a tremendous area of bone instead of placing additional bone as grafts.

In others of the series we therefore did what was demonstrated in the cases presented—filled the gap in the tibia created by the saucerization with an artificial calcium source—a combination of powdered calcium triple phosphate and calcium carbonate well mixed with the blood allowed to fill up the cavity. In these cases we not only secured bony union, but filled the tibial defect with bone, at times even above the normal tibial surface level. In one case we introduced with the calcium a phosphatase derived from rat femora by water extraction under chloroform. It showed solid union in five weeks, with X-ray evidence of new bone in the cavity. I do not recommend the clinical use of these procedures on the basis of so few results. I am merely citing these cases in brief; a further report on a larger series is contemplated which will embody a discussion of details, and from which we may be able to draw definite conclusions. I must emphasize the fact that by removing a large area of bone in this way adequate access of granulation tissue and accessory circulation is allowed to the fracture site, and that the artificial calcium source in powdered form is readily permeable by the growing tissue. It is, however, unquestionably not utilized in the form in which it is placed in the cavity, but it apparently adequately functions as a source.

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# FRACTURES WITH SPECIAL REFERENCE TO THE HIP, ANKLE AND ELBOW\*

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FROM THE SECTION ON ORTHOPEDIC SURGERY OF THE MAYO CLINIC

FRACTURES in America are today receiving better treatment than ever before. There is now an ample number of beds in hospitals for the sick and injured. The World War emphasized the fact that fractures taken care of in mass receive better care, and this has led to the institution and proper maintenance of fracture wards in most of the larger metropolitan hospitals. The American College of Surgeons and the American Medical

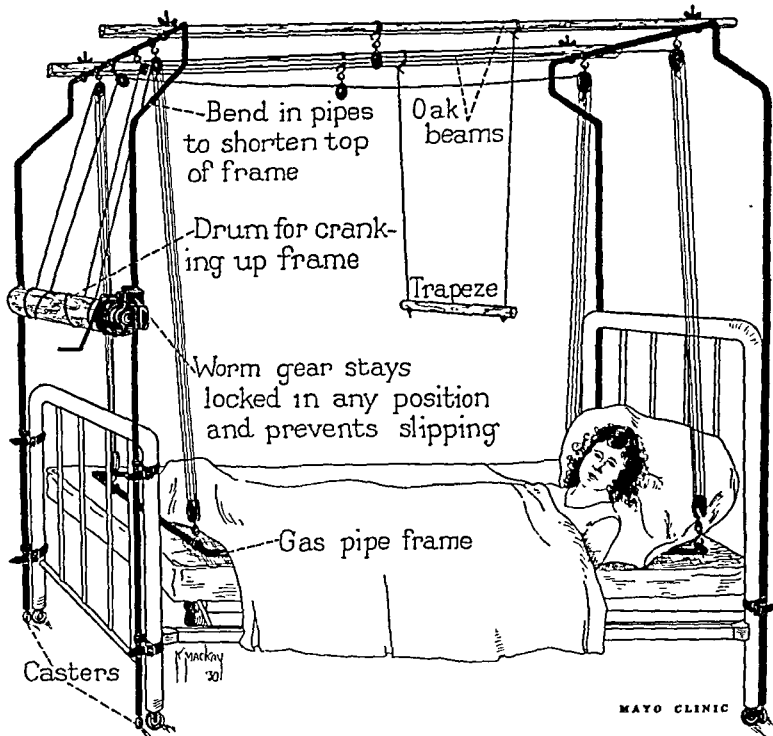


FIG. 1.—Balkan frame with elevator and trapeze.

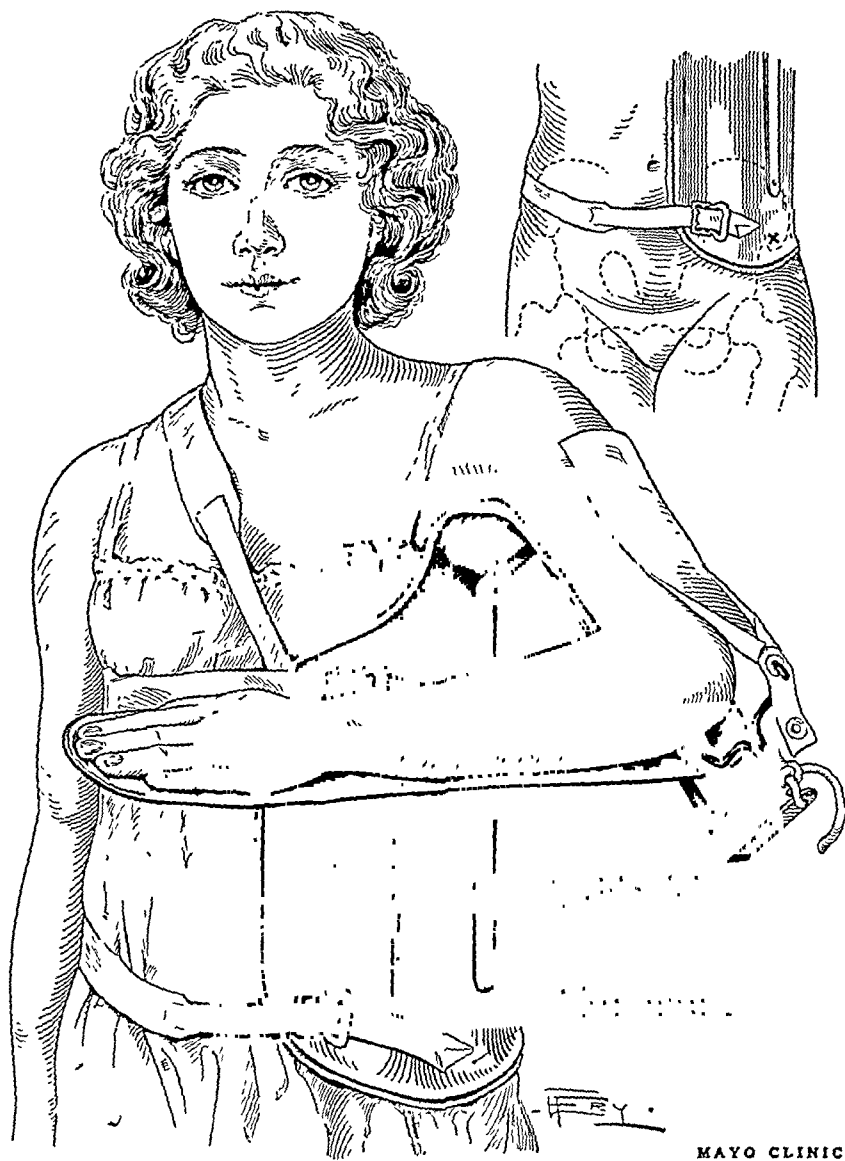
Association, through their Fracture Committees, are bringing to the attention of the hospitals the necessity of good apparatus, splints and braces for the treatment of fractures. The overhead bed frame, often called the Balkan frame, is standard equipment in most hospitals.

In the Mayo Clinic we have developed a type of frame which serves our purpose best (Fig. 1). It is a frame of gas pipe with casters. It rests on the floor, which renders it more stable because the weight of the frame, weights, and so forth, is not carried by the bedstead. With casters on the uprights, frame and bed may be rolled about on the floor. The gas-pipe

\* Presented before the Oklahoma City Clinical Society, November, 1930.

## FRACTURES OF HIP, ANKLE AND ELBOW

uprights are angled inward at the top so that the ends of the frame do not project beyond the bed, an important factor when the bedroom is small. On such a frame any kind of suspension and traction can be arranged. The elevator for raising the bed frame is a worm gear apparatus and although it elevates the patient slowly, it locks securely in any position. Overhead beams are oak instead of metal, for safety when bedside röntgenologic apparatus is used. For fractures of the lower extremity a good supply of Thomas



MAYO CLINIC

FIG. 2.—Abduction splint with traction post.

extension splints, of different lengths and with rings of different sizes, is necessary so that they may be readily available for emergency use. We have found very useful in the treatment of fractures of the shoulder and of many fractures of the shaft of the humerus, a modification of the airplane splint which has on it, at the bottom of the arm-piece, an extension post for traction (Fig. 2). Stock splints of this type, as made by various commercial houses, have so many adjustments that the splints are cumbersome.

Delay in the institution of treatment I consider the chief cause of poor

end-results, but a nearly equal cause, I believe to be careless treatment by recognized and standard methods. However, if a fracture is compound, often treatment must necessarily be delayed, and the procedure of choice cannot always be used. Œdema, swelling, extensive hæmatoma, laceration of skin, injury to the nerves and poor general condition of the patient due to injuries sustained in the same accident which caused the fracture, all raise problems that are difficult to solve. After the fracture is reduced, the maintenance of reduction is not always easy, and traction<sup>1</sup> in some form is often necessary. The type of treatment selected may be influenced by the social status or health of the patient, the equipment at hand, the mechanical ingenuity of the surgeon, and last but not least, the surgeon's willingness to accept the full responsibility of maintaining the fracture in its reduced condition. Patience and skill are necessary. I place patience first because no matter how skillful the surgeon may be in obtaining reduction it may go for naught if the fragments are permitted to become disengaged through faulty maintenance of position.

The advent of aseptic surgery and Röntgen-rays made possible a real departure from the standards established by centuries of practice in the treatment of fractures. Consequently, two methods have developed: reduction by open operation and reduction by the closed method. The popularity of each of the methods has risen and fallen in recent years, but the tendency now seems to be more toward the open method. An open operation to reduce a simple fracture which, however, may not be simple so far as reduction is concerned, is attended with little risk to the patient. I believe the open method will be used with increasing frequency in simple fractures, because due to the increase of industrial pursuits, and rapid transportation, with their hazards, fractures are far from simple in the literal use of that word.

The conservative or "closed" method of treatment entails the use of apparatus, simple in mechanical principle. However, it has been my experience when visiting large fracture wards that are not only well manned but have every mechanical facility, too often to see apparatus that is perfect in design and conception doing anything but what it should be doing, because of some trivial interference. This, occurring even under the best of conditions, makes one realize the difficulties in using apparatus that is intended to be both corrective and retentive. Unless the surgeon is willing to give sufficient personal supervision to the exacting details incident to the carrying out of the closed method, it may be that, for him at least, better results by open reduction of the fractures will be obtained. Usually the apparatus has first to reduce the fragments and then to hold them in position. After open operation and reduction the apparatus merely retains a position obtained.

About twenty years ago, a committee appointed by the British Medical Association<sup>3</sup> spent a great deal of time tracing a number of patients who had had fractures, endeavoring to ascertain whether the best results were obtained by the closed method or by the open method. It is evident, in reviewing their report and reading between the lines, that although the

committee was convinced that better results had been obtained by the open method, because of the danger of broadcasting to the profession in general, and thus encouraging the use of a method that in untrained and unskilled hands is potentially dangerous, they did not stress the facts really obtained. A few years later, the American Surgical Association<sup>5</sup> made a similar review, but the results, as they found them, were so disappointing that they failed to publish the outcome of their inquiry; the report lies buried in the little-read transactions of the society.

In our practice in the Mayo Clinic, we hold no preference either for the closed or for the open method, but adapt the method to the fracture under consideration. If the operative open method is to be used, it should be carried out at once and not after reduction has been attempted by vigorous manipulations. We have long abandoned the view that the operative method should be used only after conservative efforts have failed. On the other hand, we are also far from the point of advising operative interference for all fractures. Since the institution of a hospital service ready to take care of fractures at any time, day or night, our fracture service has steadily grown to a considerable size for an agricultural community.

Skeletal traction is once more coming more into prominence. The work of Boehler, with his placing of small wire-like pins under local anæsthesia, and the method of Kirschner, with his special apparatus for introducing fine wires, have made possible more free use of the method. Orr for many years has treated fractures by the same principle. Steinman pins are large and tend to produce irritation at the point of contact with soft tissue. There can be no doubt that skeletal traction, properly applied, is superior to any other form of traction employed. It may be used to advantage in certain fractures of the os calcis and of the lower end of the tibia, involving the joint, and in fractures of the lower end of the humerus, when there is much comminution and involvement of articular surfaces. However, skeletal traction in unskilled hands may lead to serious infection.

In a paper of this nature it is impossible to review the many different types of fractures that could be considered profitably. Therefore I have selected fractures of the hip, the ankle and the elbow for consideration, because they are in situations where poor results are likely to lead to serious disability.

### FRACTURES OF THE HIP

Fractures of the neck of the femur, and I am speaking of the intra-capsular and not of the trochanteric type, usually occur in elderly persons and indirectly cause the death of many patients. Whitman, who for many years has advocated his abduction method, has gradually convinced the profession of its merits, so that it is now more or less accepted as the standard treatment. Attempts have been made in the last few years, particularly by the American Orthopædic Association, to find out what the results are following treatment of recent intracapsular fractures of the neck of the femur.<sup>10</sup> It is not an easy task, for many confuse the trochanteric fractures with those under consideration. The mortality rate

among patients with intracapsular fracture of the neck of the femur is high, regardless of what line of treatment is carried out. The group that I am reporting herewith is an unselected group of patients with intracapsular fracture of the hip, taken as they came in, regardless of age, condition, and so forth. If one were to select the cases of patients who were young enough and well enough to permit satisfactory treatment, the mortality rate would be much lower. The number of patients aged less than sixty years in this unselected group is fifteen with a mortality rate of 13.3 per cent.; the number of patients aged more than sixty years is twenty-seven with a mortality rate of 14.8 per cent. (tabulation). The mortality rate for the combined age group was 14.2 per cent. Any death which occurred during the period of treatment has been included, regardless of whether or not the patient was in hospital. One patient died of appendiceal abscess three months after the

## FRACTURES OF THE NECK OF THE FEMUR

|                              | Fifteen patients less than 60 years.<br>Males 7; females 8   | Twenty-seven patients more than 60 years.<br>Males 9; females 18   |
|------------------------------|--|--|
| <i>Treatment</i>             |  |  |
| Abduction<br>(Whitman) . . . | 10   | 14   |
| Traction . . . . .           | 1  | 5  |
| Spica cast . . . . .         | 2  | 7  |
| Open reduction .             | 2  | 1  |
| <i>Results</i>               |  |  |
| Bony union . . . .           | 10 (76.9 per cent.)  | 13 (54.1 per cent.)  |
| No union . . . . .           | 1  | 7  |
| Not known . . . .            | 2  | 3  |
| Died . . . . .               | 2 (13.3 per cent.)<br>One died of pneumonia after sixteen days and one of appendiceal abscess after three months | 4 (14.8 per cent.)<br>One died of shock after three days, one of pneumonia after three weeks, one of pulmonary embolism after thirty-two days, and one of uræmia after six weeks |

accident; he had been sent to his home in the country for convalescence but failed to reënter the hospital before rupture of the appendix. One patient died of pulmonary embolism thirty-two days after the accident; one of shock in three days; one of uremia in six weeks; one of pneumonia in sixteen days, and one of pneumonia in three weeks. Excluding from consideration the patients who died under treatment, and basing our percentage of good results on those who survived and those concerning whom results are known, it was found that bony union was obtained in 90 per cent. of the patients aged less than sixty years and in 65 per cent. of those aged more than sixty years. On the other hand, if the patients are not divided into age groups and the patients who died are counted as failures, excluding only those concerning whom the result was unknown, the number would be thirty-seven, twenty-three (62.1 per cent.) of whom obtained bony union. If the patients who died and those who were not traced are excluded, the number would be thirty-one, and the percentage of bony union for the entire group would be 74.1. It seems fairest, however, to include the dead as failures and leave out only

those concerning whom the end result is not known. Therefore, in this series bony union was obtained in 76.9 per cent. of patients aged less than sixty years and in 54.1 per cent. of patients aged more than sixty years. This percentage, I believe, is representative of the average results in any given group of cases in which treatment was carried out under conditions of good hospital equipment, and so forth. Campbell, with a large experience, has reported a high percentage of successes following the Whitman method. There may be isolated instances in which careful selection of cases, and so forth, may raise the percentage of successful results, but I believe that any real improvement in results will have to be obtained by some other method than those in use now.

Smith-Petersen is advocating that most patients with fracture of the hip be operated on. He inserts a metal, flanged nail and his results thus far have been most encouraging, but I think we should await further evidence from him before carrying out more or less routinely any such treatment. However, there is no reason why the elderly patient should not have the advantages of modern surgery, for it is astonishing how well the aged tolerate proper surgery. Perhaps we have been too conservative.

When a fracture of the neck of the femur is firmly impacted, union may occur without any treatment, and I have no doubt that many patients with injuries to the hip have undiscovered impacted fractures of the hip which heal promptly. Too often, however, the opposite is true; no diagnosis is made and the result from lack of treatment is non-union. Several years ago, in reviewing the cases of ununited fractures of the hip observed at the clinic, I found that of a large series not one patient had had anything approaching proper treatment. Nevertheless, we must acknowledge that in spite of the best of treatment, non-union may result. If the physician who is called on to treat a patient feels that he cannot properly carry out the necessary treatment rigidly, he should refer the patient to someone who can. Treatment according to the method of Whitman demands fixation in a cast for twelve or fourteen weeks, with the leg in abduction and the foot inverted, and although much can be done by good nursing to alleviate the discomfort of the patient, the treatment is far from a comfortable experience. Fall in blood-pressure occurs and there is danger of pulmonary embolism. We frequently whip up the circulation with thyroid extract and with a system of exercises for the arms as suggested by Walters. A troublesome convalescent problem is the stiffness of the knee; so the shorter the period of fixation of the knee the better. Far too often, the history given is that the abduction treatment was started but that the cast either broke, or that, at the insistence of the patient or his relatives, it was removed at the end of a month or six weeks. The cast should not be removed in less than three months, and no weight-bearing should be permitted in less than six months, and only then when the röntgenogram gives evidence of union. Protection may be necessary for twelve to eighteen months.

The following reports of cases will bring out some of the points that I wish to emphasize:



CASE I.—*Fracture of the necks of both femurs, with excellent result.* A woman, aged sixty-eight years, fell on the pavement in July, 1928, and fractured her left hip. Under anæsthesia the deformity was reduced, normal length was obtained, the leg was held out in forced abduction, the foot was rotated inwardly, so as to bring the trochanter up to a more anterior position, and a spica cast was applied which extended from the thorax to the toes on the affected side and to the knee on the other. A röntgenogram, taken four months later, gave evidence of good bony union of the neck of the femur on the left. The patient was then allowed to be up on crutches, with a high-soled shoe on the right foot to prevent weight-bearing on the left. While she was walking along the corridor, using crutches, with a nurse by her side, she slipped and fell, over against the wall, but was caught before she fell to the floor. Pain in the right hip followed, and a röntgenogram gave evidence of a crushing fracture of the portion of the neck of the femur just beneath the head with no marked displacement. The patient was put to bed and the position was maintained in a Thomas splint on the right leg for three or four weeks and then movement



FIG. 3.—Fracture through neck of left femur firmly united. Compression fracture of subcapital portion of neck of right femur. Excellent function in both hips.



FIG. 4.—Fracture of neck of femur with firm bony union in three months.

was begun. She gained rapidly, all pain disappeared and weight-bearing was permitted on the leg within two months from the time of fracture; crutches were used, but no elevation. The patient has made full recovery and daily attends to her business as proprietor of a store; she is on her feet a great deal with no discomfort. She walks without limp or pain (Fig. 3).

Crushing fracture of the sound hip, when the patient was allowed to be up, has happened in several cases and may be an argument against prolonged use of the double spica. Prolonged fixation may cause sufficient osteoporosis to weaken the bone for weight-bearing.

CASE II.—*Fracture of the neck of the femur with rapid union in a case of pernicious anæmia and a cardiorenal syndrome.* A woman, aged fifty-five years, sustained a fracture of the neck of the left femur in February, 1916. She was treated according to the method of Whitman, as described, with an excellent result. Fig. 4 shows firm bony union after three months, the most rapid union I have ever seen following a fracture of the hip. This quick healing occurred in spite of the fact that the patient was suffering from pernicious anæmia, hypertension, and chronic nephritis. The patient lived for two years following the fracture with excellent function of the hip. She succumbed to anæmia.

## FRACTURES OF HIP, ANKLE AND ELBOW

One occasionally sees, in a case of chronic nephritis, rapid healing of fractures, just why I do not know, but there seems reason to believe that there is more diffusible calcium available in the blood of a patient with nephritis than of a person with normally acting kidneys.<sup>13</sup>

CASE III.—*Fracture of the neck of the femur, with firm bony union but with subsequent arthritis.* A woman, aged fifty years, was treated for fracture of the neck of the femur. Firm, bony union occurred, but two years afterward she presented atrophy and roughening of the head of the femur, leading to restriction of motion (Fig. 5).

I do not know how the results in this case could have been prevented. Nourishment of the head of the femur is obtained through several channels. Santos believes that the ligamentum teres is more often concerned with the nourishment of the head than we had thought. It is a fact that impairment of nourishment of the head of the femur may result from fracture of the neck and still be no great obstacle to bony union. Santos believes that he is able, by radiographic studies, to tell, in cases of non-union, whether or not the head is viable.



FIG 5.—Firm bony union following fracture of neck of femur but disability resulting on account of changes in head of femur.



FIG 6.—Firm bony union seven months after reduction with the head in valgus position

CASE IV.—*Fracture of the neck of the femur; reduction accomplished with valgus position of the head.* A woman, aged sixty-four years, sustained an intracapsular fracture of the right hip. It was reduced by the Whitman method, and it was possible, as is often the case in thin, elderly women, to overstretch the leg and produce enough lengthening so that the head should be slipped onto the neck in a valgus position. I believe that the valgus position of the head, when it is possible to obtain it, is favorable to the development of rapid and firm bony union. Fig. 6 represents the firm bony union seven months after reduction.

CASE V.—*Open operation for recent fracture of the neck of the femur and use of beef-bone peg.* A woman, aged fifty-five years, came to the clinic with a fracture of the neck of the femur of two days' duration. I attempted to reduce it by the Whitman abduction method, but there was a tendency for the lower fragment to slip up a little and the feeling of bony solidity one has when the fragments are thoroughly locked was not present. Accordingly the joint was opened and a badly comminuted fracture was found. So much of the articular surface was comminuted, and the capsule was so turned in between the fractured surfaces, that there was not more than a centimetre of bony contact between the head and the neck. I dissected out the tissue from between the fragments and placed a beef-bone peg through the trochanter and neck into the head, and held the leg in abduction in a plaster-of-Paris case.

Figure 7 represents the excellent result two and a half years after the operation; the beef-bone peg is still in position and shows very little evidence of absorption.

#### NON-UNION OF THE NECK OF THE FEMUR

Because of its relative frequency I shall consider briefly those patients whose hips fail to unite and who have definite non-union. They are disabled because of lack of skeletal support; weight-bearing is carried on by ligamentous and muscular support. Pain is variable, but may be the most distressing symptom. The problem presented to the surgeon is to furnish skeletal support with maximal motion. Following the primary wave of enthusiasm for the bone-grafting treatment of ununited fracture of the neck of the femur, there was a swing of the pendulum toward the so-called reconstruction operations. This was natural, because an operation for non-union of the hip, wherein a bone graft is used, is difficult and tedious, and



FIG. 7.—Recent fracture reduced and held by beef-bone peg. Rontgenogram two and a half years later. Persistence of the beef-bone peg may be noted.



FIG. 8.—Condition eight years after open operation and insertion of fibula as a graft for non-union of two years' duration. Persistence of bone graft may be noted. Excellent function.

calls for all the skill the surgeon possesses. The risk incident to the operation, and the long confinement afterward, are factors that cannot be disregarded. If the operation is a failure the patient has made a big sacrifice, and such a result is a keen disappointment to him and to his surgeon. Series of cases have been recorded in which 75 per cent. or more good results have followed the use of a bone graft for non-union of the neck of the femur; therefore it is established that in properly selected cases good results may be obtained.<sup>5</sup> Albee recently reported a series with over 90 per cent. successes.

The patient should be preferably under fifty-five years of age, in good health, and of the vigorous type. A meticulous operative technic must be developed, and good access to the fractured surfaces must be obtained, so that freshening and fitting of them may be carefully carried out, aided by visual inspection. A good-sized graft should then be taken, either a full segment of the fibula or a piece from the tibia, and this should be put in the channel prepared for it, through the trochanter, through the remnant of the neck, and up into the head. If the graft is taken from the upper end of

## FRACTURES OF HIP, ANKLE AND ELBOW

the tibia, curettefuls of the spongy bone near the epiphyseal line should be removed and packed as a sort of cement around the graft to fill in any gap that might exist between the freshened head and the freshened neck. Bone taken from near the epiphyseal line is rich in bone-forming properties.

If the patient is too old and is not thought fit for such a radical procedure as grafting of bone, or if too much atrophy of the head and neck is present, the reconstruction operation of Whitman gives good functional



FIG. 9.—Skeletal traction for comminuted fracture of lower end of tibia. Side rods with crutched ends to force down the pin through the os calcis (Gillette).

results. Also, when the hip-joint has been opened, difficulties may be encountered which will prevent satisfactory freshening and fitting of the head to the neck of the femur. These difficulties may be impossible to surmount within a time commensurate with safety. In these cases I believe that the Whitman reconstruction operation should be carried out. Viability of the head often has been mentioned as being of extreme importance. It is difficult to tell when the head of the femur is dead for even when it is living it may be impossible to demonstrate bleeding by freshening it. Not infre-

quently I have been agreeably surprised to find that the head of a femur, which I had thought was dead and of little use, would function properly after a bone-grafting operation had been performed and to find that the head did not show late changes on resumption of weight-bearing. This is illustrated by the case of a man, aged fifty-eight years, who suffered from non-union at the hip for two years. The fibula was used as a graft, and Fig. 8 shows the condition eight years after operation and demonstrates persistence of the bone graft over a period of eight years. The patient has full function of the hip, with no limp. This case furnishes some clinical evidence to refute the statement that bone grafts are absorbed and do not persist and live in their original form.

#### FRACTURES OF THE ANKLE-JOINT

Fractures of the ankle-joint may be particularly difficult to treat and may lead to great disability. This is illustrated by the case of a young man

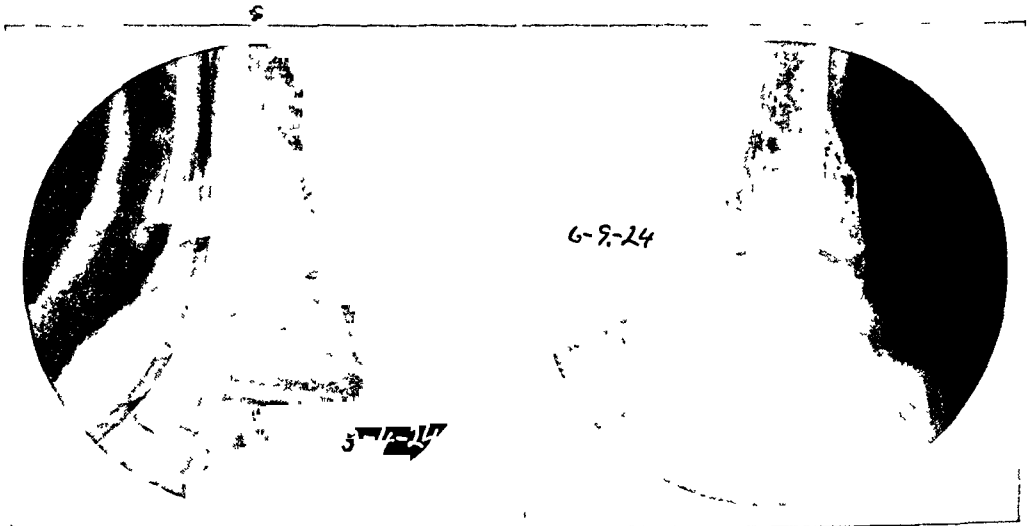


FIG. 10.—Fracture of ankle with posterior displacement of astragalus. The posterior fragment is so large that the convex surface of the astragalus finds inadequate resting place in the remaining concave arch in the tibia.

FIG. 11.—Ankle shown in Fig. 10, four months after reduction. The beef-bone screw may be noted.

who had a compound, comminuted fracture of the lower end of the tibia. Although the joint itself was not opened there was much excoriation of skin, with considerable subcutaneous hæmorrhage and œdema. A pin was placed through the os calcis and the apparatus described by Gillette was used (Fig. 9). Rods, crutched on the ends to fit over the pin, the opposite end fitting into cannulas with set screws, were fitted into the case. Force was exerted by screwing up the set screws, thus forcing the pin, and hence the foot, downward. For such procedures the case must include the foot and leg and must extend well up onto the thigh, with the knee flexed. A good deal of padding must be placed on the flexor surface of the thigh so that pressure will not cause necrosis. This patient was very comfortable, good line was maintained, and although the comminution produced some broadening of the ankle the final result was excellent.

## FRACTURES OF HIP, ANKLE AND ELBOW

Pott's fracture, with tearing of the interal lateral ligament or chipping off of a portion of the internal malleolus, and fracture of the fibula 5 or 8 centimetres above the malleolus is familiar to all. There is no posterior displacement of the foot, and the malposition is merely one of valgus. Good results are readily obtained if the deformity is corrected, and the extremity is put up in a plaster-of-Paris case extending from the knee to the toe, with the foot in slight inversion so as to push the astragalus back into its normal position and if the concave upper surface of the astragalus as shown in an antero-posterior röntgeno-gram is made to fit into the slightly convex surface of the tibia.

Fracture in the same region, with posterior displacement of the foot, known as Cotton's fracture, is more formidable. There is fracture of the internal malleolus, or tearing of the internal lateral ligament, and fracture of the fibula. However, in addition there is a longitudinal, oftentimes spiral, fracture which extends upward for several centimetres, through the articular surface of the tibia into the shaft, with posterior and upward displacement of the posterior fragment of the tibia. This permits the astragalus, and thus the whole foot, to slip backward. Reduction and maintenance of correction of this type of fracture is comparatively easy, if the posterior fragment of the tibia is small. The röntgenogram made from the lateral aspect should demonstrate that the normally convex surface of the astragalus has a sufficient resting place in the concave surface of the tibia to prevent it from slipping backward after reduction. If, however, the line of fracture is sufficiently far forward so that this resting place cannot be secured, then it is exceedingly difficult to hold the foot forward in the proper position because the upward pull of the muscles on the foot will pull the astragalus against the articular surface



FIG. 12.—Same ankle as shown in Figs. 10 and 11 four years later. Note entire absorption of beef-bone screw.

of the tibia and displace the tibial fragment again posteriorly. Division of the tendo achillis may help, but if that fails it is necessary to perform an open operation and by some means to fix the posterior fragment of the tibia to the anterior fragment of the tibia, thus restoring the arch for the reception of the astragalus.

This is illustrated by the case of a woman who sustained this type of fracture. Fig. 10 shows the foot as it was held in the cast after closed reduction, but the deformity is not reduced. Fig. 11 shows the posterior fragment of the tibia restored to its normal position and held in place by a beef-bone screw, and the astragalus staying in position. The patient obtained an excellent result (Fig. 12).

When weight-bearing is permitted following a fracture of the ankle, precautions must be taken to see that the foot is not allowed to assume a valgus position. By raising the inner side of the sole and heel the foot can be held in slight varus. This is especially necessary if patients are heavy.

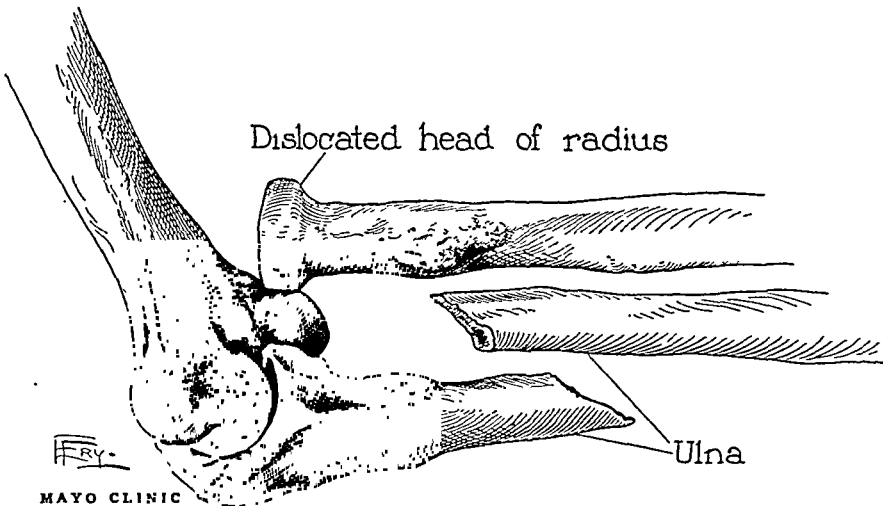


FIG. 13.—Fracture of ulna with dislocated head of radius.

#### FRACTURES OF THE ELBOW

Fractures of the elbow, common in childhood, are in reality usually fractures of the lower end of the humerus. That is, they constitute either an epiphyseal separation, or a fracture just above the epiphysis, with posterior displacement of the lower fragment and anterior displacement of the upper fragment. If they are left unreduced, marked limitation of motion results; there is inability to flex the elbow to a useful angle and also lack of extension. Fractures of the head of the radius may result in marked limitation of pronation and supination. It is surprising how much comminution of the radial head may be present and yet show but little in the röntgenograms. Therefore, if there is any reason to believe that a fracture of the head of the radius is badly comminuted, early excision of the head is indicated. Early excision results in excellent function, whereas late excision is often disappointing. A disabling fracture, more common in adults, that involves

## FRACTURES OF HIP, ANKLE AND ELBOW

the elbow-joint, occurs through the upper third of the ulna, with secondary dislocation of the head of the radius (Fig. 13). Such a fracture dislocation is best treated by an open operation. The ulna should be held in place, if necessary, by some form of internal splintage, and the elbow should be flexed somewhat more than a right angle with the hand in full supination. When a fracture of the lower end of the humerus is seen early, before swelling develops, it usually can be reduced and held in good position if the elbow is acutely flexed and is held either by a plaster-of-Paris case or by a strip of adhesive tape placed around the forearm and arm. When these fractures are seen late, after callus has formed (Fig. 14), there is nothing to do but open the joint by a posterior incision, correct the alignment, and hold the fragments in position either by the acutely flexed position or by aid of a beef-bone screw (Fig. 15). Fig. 16 shows an excellent result three years after operation in a case so treated. In the adult, particularly if the fracture

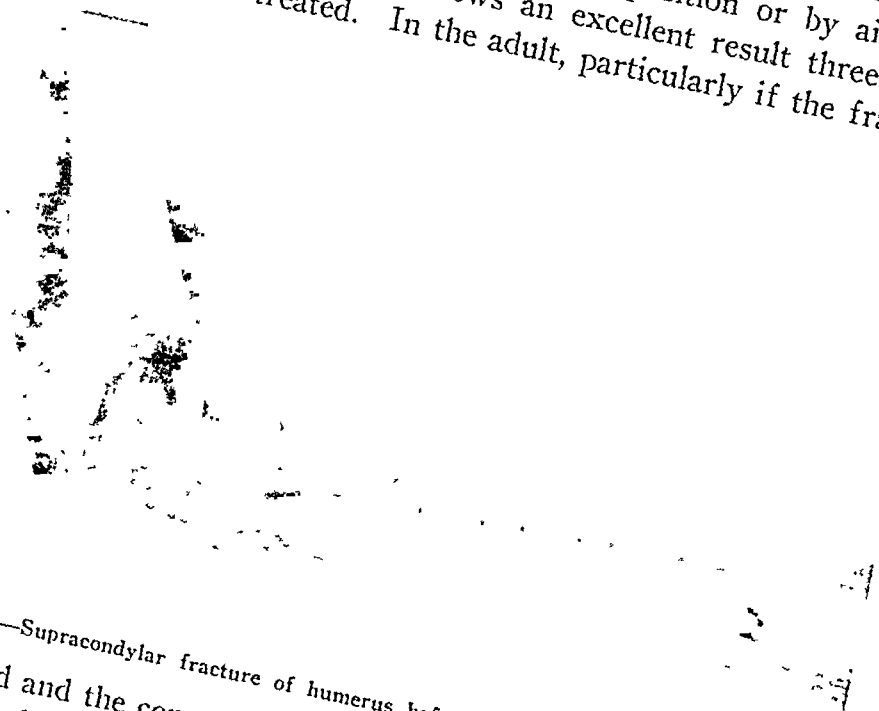


FIG. 14.—Supracondylar fracture of humerus before open reduction.

is badly comminuted and the comminution involves the articular surface, it is sometimes impossible by manipulation, or even by open operation, to restore the fragments to anything like normal position. In such cases, skeletal traction, applied on a humeral splint, by putting a wire through the olecranon process, gives as good control as can be obtained. Swelling is the great hindrance in fractures of the elbow, and may compel one to abandon a good position to prevent the development of ischæmic paralysis.

*Ischæmic paralysis of the forearm* is seen far too often. It may and does occur in the lower extremity, but the same degree of disability does not ensue. Following reduction in fractures of the elbow, an acute, flexed position of the elbow is necessary in most cases and it is this position which may lead to sufficient pressure on the superficial veins of the forearm to cause venous stasis. As the swelling increases and stasis further occurs, ischæmic paralysis rapidly develops, for it takes only a comparatively short



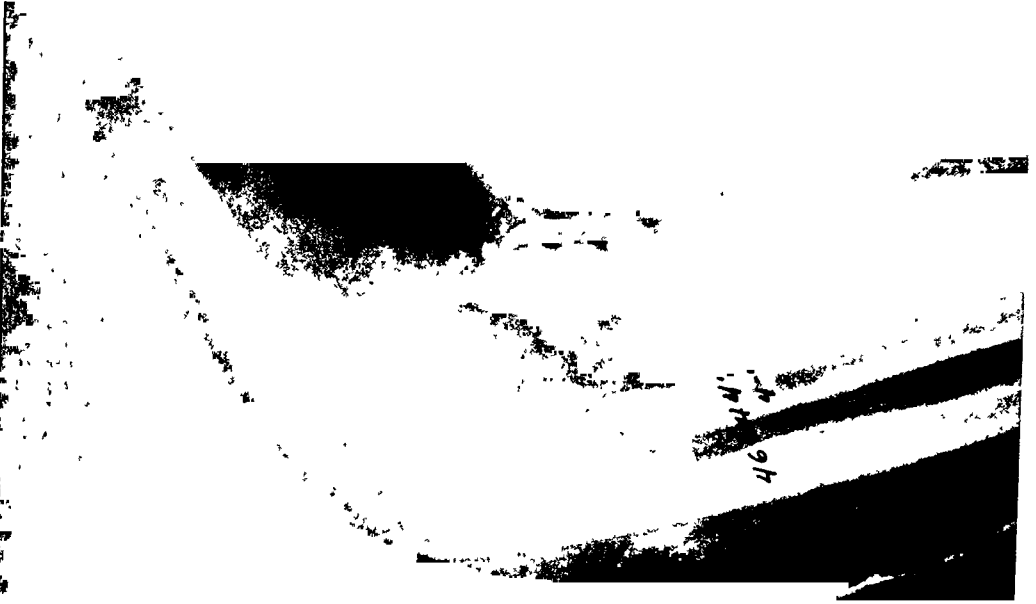


FIG. 15.—Same elbow as shown in Fig. 14 after reduction held by beef-bone screw.

time to bring on ischæmia. Severe pain, particularly if it is associated with swelling and discoloration, should receive prompt attention. Any constricting dressing should be promptly loosened, and position should be disregarded

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FIG. 16.—Seven months after reduction full function of elbow. Same elbow as shown in Figs. 14 and 15.

if necessary to restore circulation. Ischæmic paralysis, however, may occur without any constricting band or bandage having been applied; hæmorrhage within the muscular compartments may be the cause. If such is the case,

## FRACTURES OF HIP, ANKLE AND ELBOW

multiple small incisions should be made without delay to allow the encapsulated blood to escape. It is most distressing to see a child, röntgenograms of whose arm give evidence of excellent reduction of a fracture of the elbow and normal position of bony parts, but whose hand and forearm are hopelessly crippled by ischæmic paralysis. When paralysis has developed, treatment is uncertain, long and tedious, and often unsatisfactory. The Robert Jones method is most used and is carried out by a series of splints which gradually stretch the fingers from flexion into extension and then removal of bone and lengthening of tendon, have been used in resistant cases with indifferent results. Meyerding has reviewed and reported our cases. The prognosis depends entirely on the amount of muscle that has been permanently injured. Range of motion is determined by the elasticity and contractility possible in the remaining muscle. Muscle once destroyed is never fully replaced by like tissue, but by fibrous tissue.

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# MALUNION OF FRACTURES OF THE FEMUR \*

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SCUDDER<sup>1</sup> states a good recovery after a fracture of the femur should show: (1) Correct alignment; (2) full length; and (3) functional use of all joints.

The Committee of the American Surgical Association<sup>2</sup> puts the requisites for satisfactory results as follows: (1) Firm bony union; (2) the long axis of the lower fragment is either directly continuous with that of the upper fragment, or is on nearly parallel lines, thus preventing angular deformity; (3) the anterior surface of the lower fragment maintains nearly its normal relation to the plane of the upper fragment, thus preventing undue deviation of the foot from its normal position; (4) the length of the limb is exactly equal to its fellow, or the amount of shortening falls within the limits found to exist in 90 per cent. of healthy limbs: namely, from one-eighth to one inch; (5) lameness, if present, is not due to more than one inch shortening; (6) the conditions attending the treatment prevent other results from those obtained.

Variations from these standards may be grouped as follows: (1) Non-union; (2) bowing or angulation in any direction; (3) shortening; (4) rotation; (5) instability of joints; (6) displacement of fragments; and (7) stiffness of joints.

*Definition of Malunion*—With the exception of non-union, any one of these groups of defects may be present to a slight degree and still a good functioning limb obtained. If, however, in a given case, union of the fragments takes place in such a manner as to seriously interfere with function, then we may call this a case of malunion.

Jones<sup>3</sup> states that malunion is more common in the femur than in any other bone in the body. He also states that malunion can always be prevented. To his latter statement we must take exception. Nearly all cases are preventable, but some are not.

For a study of malunion I have been able to assemble thirty-two cases (Table I) seen by my colleagues and myself in Bellevue Hospital, of New York, and the Hospital for Ruptured and Crippled. Most of these cases were admitted already with malunion, some of them developed under our care. (See Table I.)

*Causes of Malunion*.—The causes of malunion of the femur may be grouped as follows:

1. Errors in the initial treatment, or in reduction of the fracture. Case

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\* Read before the Section of Surgery of the New York Academy of Medicine, May 2, 1930.

## MALUNION OF FRACTURES OF FEMUR

TABLE I

| No.                   | Age    | Site                        | Original Treatment  | Cause Malunion  | Type Malunion  | Ins. Short |
|-----------------------|--------|-----------------------------|---|---|--|------------|
| <sup>1</sup><br>S.U.  | 7 wks. | Mid. $\frac{1}{2}$          | Plaster paris, foot by car.   | Mother removed plaster paris case.  | Anterior lateral bowing marked.  | 1½"        |
| <sup>2</sup><br>D.K.  | 41     | Mid. $\frac{1}{2}$          | Closed reduction, ether, plaster paris for 8 weeks and no union—interposed muscle.<br>2. Bone inlay and plaster paris spica.  | Slipped in plaster paris and hematoma after bone inlay.                                 | Overlapping, considerable callus; moderate angulation.                               | 1½"        |
| <sup>3</sup><br>C.S.  | 12     | Mid. $\frac{1}{2}$          | Plaster paris and traction.   | Slipped in plaster paris.   | Anterior lateral angulation. Only 20° flexion in knee.                               | 1¾"        |
| <sup>4</sup><br>D.D.  | 45     | Low $\frac{1}{2}$           | Plaster paris 3½ weeks; then baking and massage. Supracondylar fracture.  | Immobilized only 3½ weeks.  | Anterior medial angulation. Relaxation ligaments knee.                               | 2"         |
| <sup>5</sup><br>B.G.  | 19     | Mid. $\frac{1}{2}$          | Tongs twice, then plaster paris.  | Tongs slipped.  | Marked anterior bowing; large amount callus.   | 2"         |
| <sup>6</sup><br>R.W.  | 23     | Mid. $\frac{1}{2}$          | Suspension 4 days; plaster paris 5 weeks; open reduction and Lane plate, up in wheelchair 6 weeks; slipped and 3rd plaster paris 7 weeks, bowing; osteotomy and plaster paris 4 weeks. Crutches and cane—16 months. | See treatment of patient. Position not maintained till union took place.                | Marked lateral bowing. Large amount callus.  | 2"         |
| <sup>7</sup><br>A.Sr. | 29     | Low $\frac{1}{2}$           | Traction—10 weeks.  | Bowing after traction released?   | Marked lateral bowing cavus of foot. Marked limitation rotation.                     | 3¼"        |
| <sup>8</sup><br>A.Sy. | 28     | Mid. $\frac{1}{2}$          | Traction—duration not known.  | ? Traction removed too soon and overweight. Lung abscess developed soon after accident. | Double fracture, marked anterior lateral bowing. Equinus foot.                       | 2"         |
| <sup>9</sup><br>A.Ss. | 47     | Mid. and Upp. $\frac{1}{2}$ | Plaster paris spica.  | Never reduced.  | Marked limitation motion knee and hip; overlapping.                                  | 3"         |
| <sup>10</sup><br>D.S. | 20     | Mid. $\frac{1}{2}$          | (1) 3 days wooden splint.<br>(2) Suspension and traction 4 days;<br>(3) 8th day after injury manual reduction and plaster paris.<br>(4) Plaster paris removed; Thomas splint and traction 8 weeks.                  | Reduction never maintained, frequent change treatment.                                  | Backward bowing and overriding, excessive callus, only slight flexion of knee.       | 2¼"        |
| <sup>11</sup><br>H.S. | 25     | Mid. $\frac{1}{2}$          | Plaster paris 3 months.   | Slipped in case.  | Displacement of fragments, knee almost stiff. Lateral angulation. Foot almost stiff. | 2"         |
| <sup>12</sup><br>H.G. | 22     | Mid. $\frac{1}{2}$          | Wooden splints.   | Never properly reduced.   | Overriding, marked callus present.   | 3"         |
| <sup>13</sup><br>S.W. | 59     | Intra-trochanteric          | Plaster paris 6 weeks. Baking and massage 4 weeks. Closed reduction not satisfactory. Open operation followed by plaster paris, bed sore; fragment slipped in plaster.  | Primarily removing plaster paris too soon, then slipped in final plaster spica.         | Marked excess of callus, coxa vara.  | 1½"        |

TABLE I (Continued)

| No.        | Age | Site                              | Original Treatment  | Cause Malunion  | Type Malunion  | Ins. Short |
|------------|-----|-----------------------------------|---|---|--|------------|
| 14<br>A.O. | 35  | Mid.<br>$\frac{1}{3}$<br>Compound | Tong traction, after debridement.   | Compounding, osteomyelitis.   | Overlapping, osteomyelitis, displacement.  | 3"         |
| 15<br>J.G. | 52  | Neck<br>Rt.                       | Few days traction. Plaster paris 3 months, bone graft. Two subsequent hip operations, nature not known.     | Changing treatments. Improper position in casts following operations. | Coxa vara. Edema leg and foot. Excessive callus, marked adduction hip.   | ?          |
| 16<br>W.H. | 23  | Low<br>$\frac{1}{3}$              | Tong traction few days, resting in bed, then crutches.  | Tongs slipped. Patient refused re-application.                        | Overlapping, excessive callus.   | 3½"        |
| 17<br>M.L. | 15  | Mid.<br>and Low<br>$\frac{1}{3}$  | "Australian" traction 1 month.  | Traction treatment too short.   | Backward displacement of lower fragment.   | 1"         |
| 18<br>W.K. | 57  | Neck<br>Left                      | Psychosis 30 days; side splint; ether reduction and plaster spica which was removed in 5 weeks.             | Delay in initial treatment—psychosis 30 days. Spica removed too soon. | Coxa vara. Edema leg three years afterwards.   | 2"         |
| 19<br>J.W. | 14  | Mid.                              | Skin traction. Irritation skin. Then no treatment.  | Traction removed too soon when skin broke down—then no treatment.     | Overriding and lateral angulation, excessive callus.   | 2"         |
| 20<br>M.R. | 46  | Mid.<br>$\frac{1}{3}$             | Skin traction; non-union; sliding bone graft held with chromic catgut and plaster paris.                    | Cast cut too soon, slipped.   | Overriding; angulation.  | 2½"        |
| 21<br>L.B. | 60  | Petro-<br>chanteric               | No treatment 3 days, then plaster spica under spinal anaesthesia.   | Slipped in case.  | 50 per cent. limitation flexion hip. Marked thickening about great trochanter. Marked limitation abduction and rotation leg. | ½"         |
| 22<br>P.D. | 16½ | Mid.<br>$\frac{1}{3}$             | Skin traction 14 days, then plaster paris.  | Changed treatment, slipped in case.                                   | Overlapping.   | 1¾"        |
| 23<br>E.K. | 50  | Upp.<br>$\frac{1}{3}$             | Skin traction for 2 days. Tongs slipped twice, then case applied.   | Pagets disease, blood calcium 14 mgm. Tongs slipped. Slipped in case. | Marked outward displacement of upper fragment; overriding.   | ?          |
| 24<br>M.H. | 54  | Neck<br>Left                      | Plaster paris spica 3 months.   | Absorption neck.  | Absorption of neck, external rotation solid union.   | 1¾"        |
| 25<br>B.M. | 38  | Mid.<br>$\frac{1}{3}$             | Tongs 8 weeks; skin traction 30 days, case.   | Slipped while in skin traction.                                       | Displacement, overlapping, knee almost stiff.  | 1½"        |
| 26<br>G.H. | 55  | Mid.<br>and Low<br>$\frac{1}{3}$  | "Australian" traction 1 month. Tongs 11 days but wounds suppurated and tongs removed and then no treatment. | Suppurative tong wounds. Slipped when tongs were removed.             | Stiff knee.  | 2"         |
| 27<br>M.G. | 53  | Low<br>and Mid.<br>$\frac{1}{3}$  | Tongs 17 days; skin traction 5 weeks; Hennequin band about ankle 2 weeks, Thomas ambulatory splint.         | Tongs slipped.  | Angulation and overriding, marked.   | 2"         |

## MALUNION OF FRACTURES OF FEMUR

TABLE I (Continued)

| No.        | Age | Site                              | Original Treatment  | Cause Malunion  | Type Malunion                        | Ins. Short |
|------------|-----|-----------------------------------|---|---|--------------------------------------|------------|
| 28<br>L.P. | 16  | Mid.<br>$\frac{1}{3}$             | Adhesive traction 7 weeks, then crutches.   | Treatment discontinued too soon.                            | Marked angulation.                   | 1½"        |
| 29<br>T.T. | 36  | Upp.<br>and Mid.<br>$\frac{1}{3}$ | Tongs 1 month. Removed. Infected, skin traction 6 weeks.                            | Infected tongs.   | Overriding and angulation.           | 1½"        |
| 30<br>R.S. | 22  | Mid.<br>$\frac{1}{3}$             | No treatment 1 week because of shock, plaster paris spica 6 weeks. Fractured skull. | Delay in initial treatment. Slipping in case.               | Bowing and overriding.               | 3"         |
| 31<br>M.L. | 19  | Mid.<br>$\frac{1}{3}$             | Skeletal traction 9 weeks. Plaster 3 weeks, then Thomas ambulatory splint and home. | Patient did not wear ambulatory brace.                      | Angulation. Excessive callus.        | 3¼"        |
| 32         | 15  |                                   | None.   | Pathological fracture, at first not treated. Not diagnosed. | Marked coxa vara and outward bowing. |            |

II (Table I) illustrates this group. There was interposed soft parts (muscle) which the surgeon failed to recognize for a period of eight weeks, open operation was then done, the fragments slipped in the plaster case, and overlapping, angulation and one and one-half inches shortening was the final result. In another case (Case XII, Table I), the extremity was immobilized in wooden splints, no attempt being made to reduce the fracture (inconceivable these modern days). Overriding and three inches shortening was the final result.

2. Delay in initiating treatment. This may be the fault of the surgeon or the patient, or to some associated disease or injury. Case XVIII (Table I) developed a psychosis and delayed proper treatment thirty days. Coxa vara and three inches shortening was the final result. Another case (Case XXX, Table I) was in shock one week and had a severe fracture of the skull which prevented an anæsthesia and proper reduction. Bowing and overriding three inches was the final result. Cases of alcoholism and marked physical weakness belong to this group.

3. Failure to maintain proper position of the fragments till union is solid. This may be the fault of the surgeon or the patient or to some associated serious disease or injury. This is by far the largest of these groups and is nearly always the fault of the surgeon. As one reads over the history of these cases of malunion one gets the impression that the surgeon who treated the original injury was monkeying around with the case, shifting from one form of treatment to the other, unaware of the power of the great thigh muscles, ignorant of the time it takes callus to solidify, unskilled in the application and use of skeletal traction, forgetful of the fact that the thigh supports the weight of the body in locomotion, unaware that soft callus will bow when not protected by splints.

Cases illustrating these facts are too numerous to mention. Inspection of Table I is conclusive: "slipped in plaster," "tongs slipped," "suspension four days and then plaster five weeks," "traction removed too soon," "bowing after traction," "bowing after loosening of Lane plate"—all these are common remarks as one reviews the causes of malunion. Responsibility, however, in one case (Case XXXI, Table I) we will have to place on the patient. He went home wearing a Thomas ambulatory splint. He took it off at once and never again put it on. Union was not quite solid and he returned to the hospital a few weeks later with angulation and three and one-quarter inches shortening.

4. Infection at site of fracture or other parts of the extremity. This may be due to compounding, the compounding being direct or brought about by extensive soft part damage and later sloughing, or it may be due to infection following open reduction of the fracture. It is impossible to prevent infection in a goodly number of compound fractures, but infection after open reduction must be charged to the surgeon. Large hæmatomas occurring after open reduction may be regarded as mild infections, since they heal usually by secondary intention and frequently become secondarily infected,

or cause liquefaction of tissues and bone absorption. Tong or skeletal traction wounds may become infected. This we blame on the surgeon. We have seen one case of extensive, severe cellulitis of the skin where skin traction was used. The scarring was so extensive from this infection that serious disability resulted. Such an infection is also chargeable to the surgeon. The skin should have been shaved, washed, sterilized, and the adhesive or mole skin flamed.

In this group belong the following cases: (1) Case XIV (Table I), a compound injury, with osteomyelitis and three inches of overlapping resulting; (2) Case XIX (Table I) traction was removed when "skin broke down," and angulation and two inches shortening resulted; (3) Case XXIX (Table I) "infected tongs," overriding of one and five-eighths inches with angulation.

5. Absorption of the neck. Most of these cases result in non-union, or fibrous union, though some finally get bony union. It is not preventable. It is discouraging. It is slow in asserting itself. We had two such cases (Cases XVIII and XXIV, Table I). The patients apparently got bony union after absorption of neck.

6. Pathological fractures may unite in a way which is not preventable, but, to quote B. L. Coley<sup>4</sup> "displacement is greatly hampered by the presence of the tumor tissue about the site of fracture, so that marked overriding is unusual." Angulation in such cases is usually due to lack of or improper splinting, as in one case of Dr. B. L. Coley's, Case XXXII (Table I), a boy with a pathological fracture which was, before being brought to Doctor Coley, undiagnosed and untreated for several months, marked angulation and shortening being the result.

Malunion of fractures may occur in osteomyelitis, fragilitas ossium, bone cysts (most common), metastatic neoplasms, syphilitic bones, rachitis, *etc.*

7. Fractures involving the epiphysis in children may unite and grow in any direction.

8. An unnoticed fracture, particularly in the aged. These are more common about the neck of the femur. The patient may start limping or merely complain of pain at the hip or knee. Meantime, the fracture heals in a position of coxa vara or fails to heal, absorbs and non-union occurs.

9. Excessive callus. We have seen two cases in which it seemed the overgrowth of callus was largely responsible for the loss of function present. Callus also frequently contributes to loss of function, along with angulation, overriding and other deformities. Case XV (Table I) was such a case. The overgrowth of callus prevented abduction of the limb, for the broadened great trochanter impinged on the ilium when abduction was attempted. This patient had had three previous operations about the hip and hence much stimulation for bone overgrowth. It is probable also that the abduction deformity could have been prevented, had the limb been put up after these operations in more abduction. In seven of the cases operated upon the surgeon mentioned in his findings "excess callus." It seems nature throws



out enormous amounts of callus in an attempt to repair the displaced fragments.

In order that responsibility may be definitely placed we may put these causes of malunion into two groups:

A. *Preventable Causes of Malunion.*—This group makes up 80 per cent. of the causes of malunion in the series I studied. (See Table I.)

(1) Failure to recognize interposed tissue. (2) Failure to secure satisfactory reduction. (3) Delaying, in an uncomplicated case, early reduction. (4) Failure, in an uncomplicated case, to maintain proper position of fragments till union is solid: (a) slipping in case; (b) tongs slipping; (c) shifting from one form of treatment to another; (d) bowing after traction or after splints removed; (e) not using Thomas ambulatory splint in many

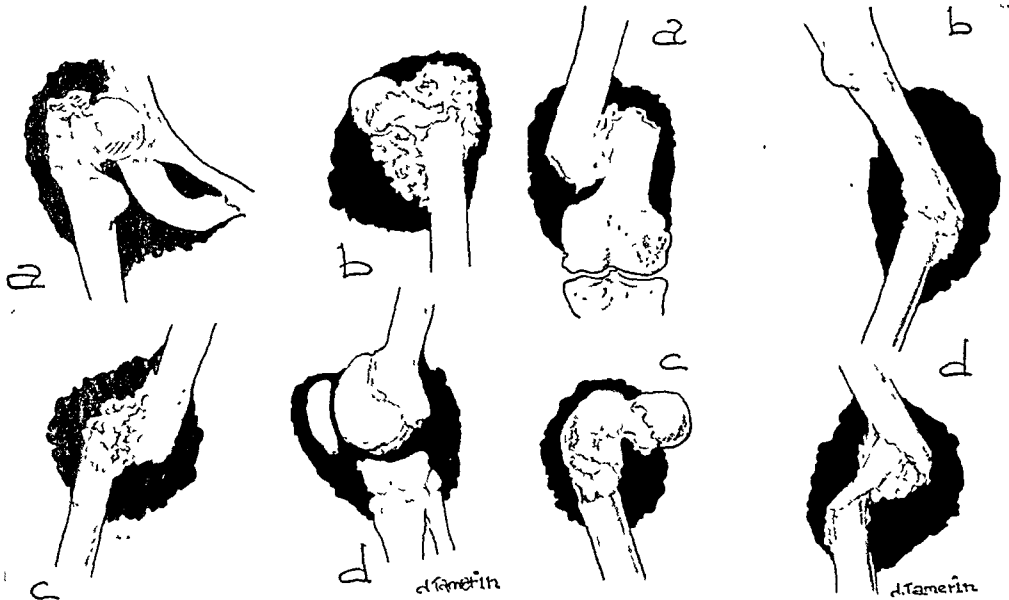


PLATE I.—Illustrating Types of Deformity.\*  
A. (Case XXIV, Table I) Coxa Vara, absorption of the neck, rotation outward as shown by prominence of lesser trochanter. B. (Case XIII, Table I) Marked excess of callus. C. (Case XI, Table I) Overlapping and displacement backwards of upper fragment. D. Displacement forward and upward of lower fragment.

\* Drawings from actual cases.

PLATE II.—Types of Deformities.\*  
A. (Case XVI, Table I) marked overlapping. B. (Case XXXI, Table I) marked angulation. C. (Case XXXII, Table I) angulation in healed pathological fracture, osteitis fibrosa cystica. D. (Case VIII, Table I) double fracture with angulation.

\* Drawings from actual cases.

cases. (5) Infection: (a) in most compound fractures; (b) in all open reductions; (c) in all tong or pin wounds; (d) of skin in skin traction; (e) hæmatomas occurring after open reduction (frequently amount to mild infections).

B. *Non-preventable causes of malunion.*—This group constituted 20 per cent. of the cases. (See Table I.)

(1) Delay in initiating treatment due to associated disease or injuries. (2) Failure to maintain proper position of the fragments is sometimes due to lack of coöperation of patient, sometimes due to associated disease or injury. (3) Infection in some compound fractures. (4) Absorption of

neck of femur. (5) Certain epiphyseal fractures. (6) Fractured hip in which patient does not seek treatment for some time. (7) Excessive callus.

*Types of Deformities* (see Plates I and II).—1. Overlapping, overriding (Table I, Cases XI, XII, XXII, XXVI).

2. Angulation or bowing in any direction (Table I, Cases I, II, III, IV, V, VI, XXXI).

3. Rotation (usually lower fragment) recorded once in thirty-three cases (Table I, Case XXIV) but was probably present in some cases and not noted on chart.

4. Excessive callus (Table I, Cases XV, XIII) more commonly associated with other types.

5. Hip, or proximal end femur: (a) loss neck femur due to absorption (Case XXIV, Table I); (b) coxa vara (Table I, Cases XXI, XXXII).

6. Knee-joint, or distal end of femur: (a) fracture into joint, one or more fragments displaced; (b) entire epiphysis displaced.

7. Displacement of shaft fragments—wide separation (Table I, Cases XIV, XXV).

8. Combinations of above types (Table I, Cases II, X, XI, XIV, XV, XVI, XVII, XIX, XXIII, XXV, XXVII, XXIX, XXX).

*Classical Operations Performed for These Various Types of Malunion* (see Table II).—1. Open osteotomy: (a) this may be done by various methods as devised by Jones,<sup>5</sup> Whitman<sup>6</sup> and others. Following the operation the limb is straightened, plaster-of-Paris spica is applied, or some form of traction. Cases so treated were IV, V, VI, VII, VIII, IX, XXXII (Table II). (b) Closed osteotomy followed by plaster. In children or in adults where union is not strong or where there is marked atrophy, osteoporosis, of femur (Cases I and V, Table II). The osteotomy is done largely to overcome bowing or angulation thereby securing better alignment.

2. Large exposure, separate fragments, may remove some of the callus present, reappose fragments, plate, bone graft, or apply skeletal traction. Cases so treated were III, IX, X, XII, XVI, XIX, XXX, XXXI (Table II). The idea in this group of cases is usually to increase the length of the extremity as well as correct the alignment. A procedure which offers much in this direction is that of Dr. LeRoy C. Abbott, of St. Louis. He has lengthened to date some fifty tibias and some twenty femurs. His results in the leg have been remarkable, an average of two inches in length being gained. In the femur 50 per cent. good results have been obtained. Recently at the Academy of Medicine, New York, Doctor Abbott showed moving pictures of two cases where a gain of four inches in length had been obtained in an extremity, two inches by lengthening the femur and two inches by lengthening the tibia. All of Abbott's cases have been in children sixteen years of age or younger, and most of them in paralytic cases, but his principles of lengthening are according to the best surgical technic and will undoubtedly in the future be given a thorough trial in certain cases of malunion of the femur resulting from trauma.

TABLE II  
*Cases of malunion operated upon*

| No.        | Age       | Type   | Treatment   | Result  |
|------------|-----------|--|---|---|
| 1<br>S.W.  | 7<br>wks. | Mid $\frac{1}{8}$<br>Anterior lateral angulation. $1\frac{1}{2}$ " shortening.                                 | Closed reduction and plaster paris spica.   | ?   |
| 3<br>C.S.  | 12        | Mid $\frac{1}{8}$ anterior lateral angulation. $1\frac{3}{4}$ " shortening, only $20^{\circ}$ flexion in knee. | Open operation, separation fragments, excessive callus removed, plated. Plate removed $2\frac{1}{2}$ months.  | Slight lateral bowing, slight limitation flexion knee.  |
| 4<br>D.D.  | 45        | Lower $\frac{1}{8}$<br>Anterior medial angulation marked. 2" shortening, relaxed ligaments of knee.            | Osteotomy— $\frac{1}{4}$ " wedge, plaster paris.  | Femur in line, brace for relaxation about knee. Knee flexion $140^{\circ}$ . Patient well satisfied. Post-operative pleurisy. |
| 5<br>B.G.  | 19        | Mid $\frac{1}{8}$<br>Marked anterior bowing, excess callus   | Forcibly broken, plaster paris.   | Flexion in knee possible to $90^{\circ}$ .  |
| 6<br>R.W.  | 23        | Up and Mid $\frac{1}{8}$<br>Marked bowing lateral, excess callus, 2" shortening.                               | $1\frac{1}{2}$ " wedge-osteotomy, plaster paris. Hematoma in wound removed 11 days post-operative.  | Discharge $2\frac{1}{2}$ months post-op. with steel and leather spica, femur in line.   |
| 7<br>A.Sr. | 29        | Lower $\frac{1}{8}$<br>Marked lateral bowing. $3\frac{1}{4}$ " shortening.                                     | Wedge-osteotomy, plated, plaster paris.   | Leg straight.<br>"Improved."  |
| 8<br>A.Sy. | 28        | Mid $\frac{1}{8}$<br>Double fracture with marked lateral and anterior bowing. 2" shortening.                   | Simple osteotomy and plaster paris. Spinal anaesthesia.   | Stable extremity, but flexion at knee only to $25^{\circ}$ .  |
| 9<br>A.Ss. | 47        | Mid $\frac{1}{8}$<br>Overriding 3" shortening. Knee almost stiff.  | Osteotomy, fragments separated, freshened ends, traction with Steinmann pin in femur.   | Marked stiffness in knee. 2 years later Bennett operation on knee, but marked stiffness in knee remained.                     |
| 10<br>D.S. | 20        | Mid $\frac{1}{8}$<br>Back bowing overriding, excessive callus $2\frac{1}{4}$ " shortening.                     | Open operation, excessive callus removed, bones separated, contraction of tissue and formation of bone prevented reduction, bones then locked and held with bone screw. | Died—four days post-operative. Gas Bacillus Infection.  |
| 12<br>H.G. | 22        | Mid $\frac{1}{8}$<br>Overriding, marked amount of callus.  | Extremely difficult open operation, excessive callus removed, tongs, fragments slipped, hematoma of wound, absorption some bone.  | No improvement.<br>One year out of boy's life.  |
| 15<br>J.G. | 52        | Intertrochanteric.<br>Marked excessive callus, coxa vara, adduction hip, arthritis knee.                       | Simple osteotomy at level lesser trochanter.  | Adduction deformity corrected. Motion in hip improved. Arthritis in knee excited and caused great disability.                 |
| 13<br>S.W. | 23        | Low $\frac{1}{8}$<br>Overlapping $3\frac{1}{2}$ ", excessive callus.   | Anterior incision, separation fragments, excision callus, plating, case. Very difficult operation.  | Died. Shock. Ten hours post-operative.  |
| 19<br>J.W. | 14        | Mid $\frac{1}{8}$<br>Overlapping 2" angulation lateral, considerable callus.                                   | Open operation, callus excised, Lane plate, plaster paris spica. Post-operative hematoma and slight skin infection.   | Some stiffness in knee.   |
| 30<br>R.S. | 22        | Mid $\frac{1}{8}$<br>Bowling and overriding 3".  | Open operation, separation of fragments, tongs 45 days, skin traction 38 days. Fragments never gotten end to end, even with 65 pounds traction.                         | After about two years' delayed union there was malunion with same conditions as before treatment.                             |
| 31<br>M.L. | 19        | Mid $\frac{1}{8}$<br>angulation, $3\frac{1}{4}$ " shortening, excessive callus.                                | Open osteotomy, removal of considerable callus. Steinmann pin in os calcis incorporated in plaster paris spica.   | Only six weeks since operation. X-rays show overlapping of 1" and callus not solid.   |
| 32         | 15        | Marked coxa vara and outward bowing. Osteitis fibrosa cystica  | Wedge osteotomy and plaster spica.  | Knee flexion to $90$ degrees. Hip had only slight motion. Brace to protect pathological bone.                                 |

3. Resection of knee when fracture is about knee-joint, with fragments greatly displaced—rarely an arthroplasty.

4. Reconstruction operation (osteotomy usually done but this operation occasionally indicated) about hip when there is malunion about head or neck of femur with ankylosis of hip, or with extensive arthritis of hip. Usually one of three types of reconstruction operation is done: Whitman,<sup>7</sup> Brackett,<sup>8</sup> or Albee.<sup>9</sup>

5. *Amputation.*—There are cases which unquestionably would be better treated in this way. The deformity is so great, or the time to restore will extend into years, or malunion with osteomyelitis or associated complications is so impossible to otherwise treat. Such a case is Case XIV of Table I. This was a case following gunshot injury. The patient refused amputation.

*Cases Actually Operated Upon with Results.*—Sixteen of the thirty-two cases of malunion studied by me were operated upon. I did four of these operations and assisted at three of them, and various ones of my colleagues did nine. Operation was advised in many more, but for one reason or another was not performed. Since the operative treatment is so important, involves so many principles and is so difficult, complete report of the sixteen cases is given:

CASE I.—Male, aged seven weeks. Middle third left femur showed anterior lateral angulation with one and one-half inches shortening. Operation May 29, 1929: Closed reduction and application plaster spica. *Comment.*—Good result and should have been at this age.

CASE III.—Female, aged twelve years. Middle third, antero-lateral angulation with one and three-quarter inches shortening. Operation August 4, 1927: Six-inch lateral incision fragments separated, some of the callus removed, ends of bone brought into alignment with considerable force, Lane plate applied, then plaster spica. October 20, 1927, Lane plate removed, the screws being loose. *Comment.*—Slight lateral bowing and some limitation of motion at knee was the final result. Border-line operative case due to age—twelve years.

CASE IV.—Male, aged forty-five years. Impacted supracondylar with marked antero-medial angulation and two inches shortening; relaxation of ligaments of knee. *Symptoms.*—Feels as if knee was being forced outward, and pain in knee. Operation March 9, 1925: One-quarter inch wedge osteotomy through lateral incision, leg straightened and plaster-of-Paris bandage applied. *Comment.*—Patient had pleurisy following operation, but this cleared up; 140 degrees flexion at knee, the limb was symmetrical, brace fitted to patient for relaxation about knee. Good result considering associated injury to knee ligaments.

CASE V.—Male, aged nineteen years. Middle third, marked anterior bowing, large amount callus, two inches shortening. Operation August 22, 1928: Femur forcibly broken under ether anæsthesia and plaster-of-Paris applied after thigh was straightened. *Comment.*—Good results with flexion at knee limited to right angle. A simple case.

CASE VI.—Male, aged twenty-three years. Upper and middle third, marked lateral bowing, large amount callus, shortening two inches. Operation April 17, 1928: Six-inch lateral incision. Bone ends appeared to be at right angles. Large amount dense callus, line of fracture could not be identified. One and one-half inch wedge removed, bone not completely divided, lower portion abducted with difficulty till wedge was closed. Plaster-of-Paris spica. *Comment.*—Eleven days post-operative a blood-clot

removed from wound, wound then healed. Discharged two and one-half months after operation with steel and leather spica brace. Exact final result not known.

CASE VII.—Female, aged twenty-nine years. Lower third right femur marked lateral bowing, three and one-quarter inches shortening, cavus of foot, marked limitation external rotation of foot. Operation October 4, 1923: Lateral incision, wedge removed at site of fracture, lower fragment abducted, fragments plated in this position, plaster-of-Paris spica. *Comment*.—Discharged with the general remark "improved." Knee with only slight motion.

CASE VIII.—Female, aged twenty-eight years, very obese. Middle third double fracture, marked antero-lateral bowing, equinus of foot, two inches shortening, had marked limp and walked with cane or crutch. Operation April 29, 1929: Spinal anæsthesia. Lateral incision, femur put in line by lifting and abducting leg, plaster-of-Paris bandage. June 3, 1929, tenotomy of achilles tendon. *Result*.—Stable extremity with marked stiffness in knee.

CASE IX.—Male, aged forty-seven years. Upper and middle thirds, transverse, three-inch overriding, two-inch atrophy thigh. Operation June 23, 1927: Lateral incision, fragments separated, ends freshened, Steinmann pin applied for traction. *Result*.—Solid bony union October 4, 1927, but marked stiffness in knee. Re-admission January 4, 1929, and a Bennett operation done on knee. February 1, 1929, knee stretched and skin broken over it. April, 1929, skin graft over knee. Final result May, 1929, solid union with marked stiffness in knee.

CASE X.—Male, aged twenty years. Middle one-third, backward bowing, overriding, excessive callus, marked limp. Operation December 8, 1924: Postero-lateral eight-inch incision, marked amount callus, fragments separated and it was found to be impossible to reduce the deformity on account of contraction and formation of bone, consequently a deep excavation cut in end of upper fragment and lower end shaped into this excavation and held by a bone screw, plaster spica. *Result*.—Died four days later, gas bacillus infection.

CASE XII.—Male, aged twenty-two years. Junction middle and lower one-third with three inches overriding, marked amount callus present. Marked limp, considerable pain in leg. Operation March 25, 1927: Gas-ether anæsthetic; lateral incision; fragments separated by chisel; ends freshened with saw; much excess callus excised—the callus extended out into the soft tissues like the fins of a fish—fracture reduced and ends apposed by traction through tongs and prying with Murphy hip chisel; wound closed; patient to ward and suspended in Balkan frame with Thomas splint and tong traction. *Result and comment*.—Even after tongs were applied on the operating table, much pulling and manhandling were also done and the fragments reduced at the time. The tissues were traumatized, large hæmatoma formed post-operative, absorption took place, then slipping of the fragments, then slow union extending over one year, and finally the patient left the hospital with the femoral fragments in the same malposition as on entrance.

CASE XV.—Male, aged fifty-two years. Intertrochanteric, large amount callus, coxa vara, adduction deformity, hip could not be abducted on account of impingement of callus and great trochanter on side of pelvis, knee almost stiff, with advanced arthritis, pain in hip. Operation March 9, 1929: gas-ether, osteotomy of femur, at level of lesser trochanter, extremity abducted to forty-five degrees, plaster spica. *Result*.—Motion (abduction) at hip increased, arthritis of knee greatly excited by operation and immobilization. Patient discharged with crutches and requesting amputation on account of pain and stiffness in knee.

CASE XVI.—Male, aged twenty-three years. Lower and middle one-thirds, overlapping three and one-half inches, much excess callus. Operation May, 1927: Gas-oxygen-ether anæsthesia, anterior incision bone fragments separated with chisel and hammer, excess callus removed, bone ends freshened, bone ends approximated with

great difficulty, Lane plate, plaster spica. *Result*.—Patient died some eight hours post-operative shock. *Comment*.—Too much was attempted in this case. The amount of callus removed was considerable, the stretching of three and one-half inches on the table was very shocking, and the time of the operation was too long—one and one-half hours. Spinal anæsthesia might have been used, plating should have been omitted, and reduction should have been slow skeletal traction.

CASE XXX.—Female, aged twenty-two years. Middle one-third, bowing and overriding three inches, heavy bone callus. Operation March 24, 1922; gas-ether, long antero-lateral incision, bone divided with chisel, excess callus excised, wound flushed with hot saline and closed. Tongs inserted in lower end of femur. Patient put in Balkan frame and Thomas splint. Traction by tongs, starting off with fourteen pounds and gradually increasing to sixty-five pounds, by the end of the seven days. This was maintained until the eleventh day when the sixty-five pounds were gradually reduced, over a period of thirty-five days, to ten pounds. On the day of maximum traction the pulse rose from ninety to one hundred and twenty where it remained until the thirty-fourth day, which was the day traction was finally reduced to ten pounds. The fragments were never brought end to end—a gain of two and three-quarter inches being at one time obtained, which was one-quarter inch from complete reduction. Tongs removed on the forty-fifth day, skin traction to eighty-third day, then Thomas ambulatory splint. Physical therapy begun. *Result*.—Patient seen one year and nine months later with “moderate overriding of fragments, bony union, outward bowing. Patient was pregnant, otherwise some operation would have been performed for malunion.”

CASE XXXI.—Male, aged nineteen years. Middle third left femur with three and one-quarter inches shortening and marked lateral angulation. Operation by Dr. H. M. B. March 7, 1930: Open osteotomy, removal of marked excess of callus, thigh straightened, position maintained by putting Steinmann pin through os calcis and incorporating this in plaster spica from chest to toes. X-rays six weeks after operation show one inch overlapping with callus (not homogeneous) being laid down. Still in plaster.

CASE XXXII.—Male, aged fifteen years. Neck of left femur. Marked coxa vara with osteitis fibrosa cystica of great trochanteric region. Operation June 1, 1929: Cuneiform osteotomy, plaster-of-Paris spica. September 6, 1929, right knee stretched and motion afterward possible to a right angle. October 10, 1929, wearing brace and crutches, very little motion in hip. Final result cannot be predicted on account of bone tumor.

*Discussion of Operative Treatment*.—These operative results are not encouraging. In children, as would be expected, the results are better. The children endure more, their tissues are softer, the reparative powers rapid and definite.

With the simple osteotomies results have been better—the operation shorter, manipulation less, less shock.

Three cases had shortening of three and one-half inches, two inches, and three inches respectively. After operation for malunion these cases ended with marked stiffness in the knees. This will happen frequently when stretching is employed to overcome shortening. Abbott has pointed this out, and advises knee motion in all cases during the post-operative treatment. Of course this is only possible by use of traction, and nearly always skeletal traction, after the osteotomy.

The worst type of malunion seems to be the one with marked deformity, marked increase in callus, and several inches of overlapping of the fragments. Results in the treatment of such cases have not been good—in fact, they

have usually been failures. Overcoming the shortening is where we have gotten into trouble. We can correct the bowing, we can remove the excess callus, we can separate the fragments, we can apply skeletal traction which will keep the joints in good condition, but if we prolong the operation by trying to immediately restore full length, then we traumatize the tissues, shock the patient, and infection, slipping of fragments, even death is liable to be the final result. Therefore, I would advise, at the time of the operation when the step comes to lengthen the extremity, that one of two procedures be adopted: (1) shorten the bone ends and appose them and be satisfied with loss in length, usually one to three inches, but with union and otherwise good function; or (2) do a "Z" or tongue osteotomy, get what increase in length slow skeletal traction will give, which may not be full length, and let union take place where it will.

Unless one has had experience with this type of case one cannot appreciate the disability to the patient and the hazards in the operative treatment and post-operative care. Most of the surgeons with whom I have discussed such cases have in the past been contented to "let the other man treat them." I believe this attitude will be changed if one of the procedures suggested above is adopted.

Operative treatment of these cases assumes that (1) there are no open wounds; (2) the skin is in good condition; (3) all infection has been cleared up at least, and better longer than, six months; (4) the patient can stand the operation; (5) the patient usually is not a child; (6) too much will not be attempted at time of operation; (7) the surgeon has a thorough knowledge of the treatment of a fresh fracture; (8) the after-treatment shall be carried out with, if anything, more skill and attention than if the case were a fresh fracture.

*Summary.*—Further points not emphasized under the discussion of operative treatment:

1. Eighty per cent. of the cases of malunion of the femur are preventable, being due to errors in treatment, usually changing treatment with slipping of fragments at the time.

2. Twenty per cent. of the cases of malunion of the femur are not preventable. Most of these cases are due to associated diseases or injuries.

3. Excessive callus at site of malunion is present in most cases. This may be an attempt of nature to repair and strengthen the deformity.

4. The treatment of cases complicated by osteomyelitis, extensive loss of bone, and associated soft part injury, is apt to extend over many years with a doubtful end-result. Therefore, amputation is to be considered in such cases.

5. The time element is a big factor in these cases. Treatment implies, first, refracture; second, prolonged treatment of the refracture (union nearly always slower in refracture cases); third, treatment of adjacent joints, muscles and tendons; fourth, often secondary operations, as tendon lengthening and stretching. All this may extend over a period of two years.

6. Arthritis of one joint in the extremity (particularly the hip or knee) is apt, at times, to overshadow any good result one might get in the treatment of malunion.

7. Spinal anæsthesia should be considered in operative treatment of these cases.

8. Absorption of neck of femur with eventual solid union, impossible to prove not bony, does occur occasionally.

I wish to extend my appreciation to the following surgeons who were kind enough to loan me records and X-rays of several cases of theirs included in this paper: Royal Whitman, Léwis Clark Wagner, Richmond Stevens, and William L. Sneed.

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# AN AMBULATORY TREATMENT OF MALLEOLAR FRACTURES

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THERE is a uniformity in the text-book teaching of the treatment of fractures of the external malleolus, with or without fracture of the internal malleolus, loosely (and frequently incorrectly) called Pott's fracture. It is to the effect that these fractures should be reduced, immobilized, either in plaster-of-Paris or other rigid splint, and relieved of weight-bearing for several weeks. Kellogg Speed,<sup>1</sup> in his text-book, is specific in advising relief of weight-bearing for eight weeks.

I have for several years been impressed with the protracted disability which frequently occurs as the result of such fractures, often with little or no displacement of the fragments. The patients at the end of six weeks or two months present a foot in which the circulation is sluggish; there is more or less infiltration, and there is a general restriction of motion in the joints of the ankle and tarsus. There is atrophy of musculature and the X-ray demonstrates atrophy of bone.

If one visualizes the sequence of pathologic changes which have occurred during that time period, the clinical picture will be made clear. One has only to observe the extensive ecchymosis that appears on the third or fourth day to realize that it signifies a considerable hæmorrhage into tissue spaces which surround a series of adjacent joints. The organization of this hæmorrhage results in the formation of adhesions, and accounts for the joint stiffness. The resumption of function under these conditions is accompanied by pain, swelling, and deformity. The foot gradually turns outward into an abducted attitude, and complete voluntary or passive adduction and reconstitution of the arch is no longer possible. This triad is generally recognized by the term "traumatic flat-foot."

The departure in treatment is based upon the observation of the disability incident to the ordinary so-called flat-foot. In the course of this very common condition, overworked adolescents and adults sometimes contract an exceedingly disabling condition called spastic or rigid flat-foot. It differs from the ordinary flat-foot in that the patient is no longer able to rise on the outer border of his foot, and thus reconstitute his arch. It is due to infiltration of the capsular structures of the joints of the inner side of the foot from chronic trauma. Long-standing cases develop adhesions which fix the joints. Clinically it is exactly comparable to the traumatic flat-foot outlined above. This paper has to do with the prevention of such a state of affairs by the early institution of movement and function. I have observed that these fractures unite when unrecognized, but with deformity.

## TREATMENT OF MALLEOLAR FRACTURES



FIG. 1.—Attitude in which the foot should be held during the application of the adhesive plaster.



FIG. 2.—The adhesive-plaster dressing applied.

Union occurs because weight is borne through the tibia and not through the malleoli. The treatment involves the following elements:

1. If there is displacement requiring reduction, this is done, and a short period of rest is allowed.

2. In fractures with no displacement, two or three days' rest in a sheet-wadding-bandage compression dressing.

3. Following this, adhesive-plaster strapping is applied with the foot in dorsal flexion and adduction (Fig. 1), and with the toes in plantar flexion. The base of the dressing is two two-inch strips which begin on the outer side of the leg, passing downward across the os calcis, adducting that bone, and then upward on the inner side of the leg to the upper border of the calf. Over this are applied successive two-inch strips, encircling the limb from the base of the toes to the upper border of the calf (Fig. 2), but leaving a small segment of the heel uncovered. The patient is then instructed to begin systematic movements at the ankle-joint. In order to be assured that he uses his tibialis anticus muscle for dorsal flexion movements, he is instructed to keep his toes plantar flexed. The dressing sufficiently fixes the fragments so that no discomfort accompanies the exercise. Weight-bearing and walking in a shoe, the heel of which has been raised  $\frac{1}{4}$  inch on the inner side, is encouraged after from three to six days after the injury.

4. The adhesive dressing is renewed every four or five days. The surgeon must be satisfied that exercises and movements are being properly carried out.

5. This régime of dressing is carried out for six weeks. Union is then sufficiently advanced so that no deformity will result. The raised heel is maintained, exercises and proper weight-bearing are encouraged until complete mobility is restored.

During the last year I have had occasion to treat seven patients in this manner—five private patients and two hospital cases. All were walking in from three to seven days; the convalescence was materially shortened, and union occurred without delay or deformity.

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# FRACTURES OF THE SCAPULA

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THE scapula has always been considered a bone which is rarely fractured. Relatively little space has been given to this subject in text-books and little information is to be found in the literature. The fracture service of the Beekman Street Hospital, New York City, from which these cases are taken, have treated twenty-three cases of fracture of the scapula during the period 1926 to 1929 inclusive. One case was bilateral, thus making a total of twenty-four fractured scapulæ during the past four years. Three of these cases had no X-rays taken, because they either died or signed a release before sufficient time had elapsed. These three, not being proven cases, will not be considered. We will include, however, a case of fractured coracoid, taken care of privately by Dr. Thomas M. Lowry. This will make a total of twenty-one proven cases with twenty-two fractured scapulæ.

The ages of the patients in this series varied from eight to sixty-three years with an average of 36.7 years. There was only one under twenty-one years; there were nine between twenty-one and thirty-five; eight between thirty-six and fifty and three over fifty. This demonstrates that the age frequency is during the active-labor period. Twenty of the twenty-one patients were males. Most of the patients were of the foreign laboring type.

The occupations may be divided as follows:

## I. *Hazardous labor*.—Thirteen cases, or 61.9 per cent.

|                       | Cases |
|-----------------------|-------|
| 1. Laborer .....      | 7     |
| 2. Painter .....      | 2     |
| 3. Longshoreman ..... | 1     |
| 4. Ironworker .....   | 1     |
| 5. Carpenter .....    | 1     |
| 6. Fireman .....      | 1     |

## II. *Moderately hazardous labor*.—Six cases, or 28.5 per cent.

|                    | Cases |
|--------------------|-------|
| 1. Helper .....    | 1     |
| 2. Butcher .....   | 1     |
| 3. Watchman .....  | 1     |
| 4. Schoolboy ..... | 1     |
| 5. Runner .....    | 1     |
| 6. Salesman .....  | 1     |

## III. *Sedentary labor*.—One case, or 4.7 per cent.

|                    | Cases |
|--------------------|-------|
| 1. Housewife ..... | 1     |

IV. *Undetermined or unknown*.—One case, or 4.7 per cent.

The history or nature of the trauma may be grouped as follows:

I. *Falling injuries*.—Sixteen cases, or 76.2 per cent.

|   | Cases |
|---|-------|
| 1. Fell four stories from a scaffold after brick fell on head | 1     |
| 2. Fell several stories from a derrick.....                   | 1     |
| 3. Fell one story.....  | 1     |
| 4. Fell one story out of a window.....                        | 1     |
| 5. Fell down a hatchway.....                                  | 1     |
| 6. Fell down eight stairs, striking arm and shoulder.....     | 1     |
| 7. Fell twenty feet from a scaffold.....                      | 1     |
| 8. Fell twelve feet, landing on shoulder.....                 | 1     |
| 9. Fell off ladder, landing on shoulder.....                  | 1     |
| 10. Fell eight feet, striking shoulder.....                   | 1     |
| 11. Fell backwards from a firetruck.....                      | 1     |
| 12. Knocked down by a truck.....                              | 1     |
| 13. Knocked down by an automobile.....                        | 2     |
| 14. Knocked down by a taxi-cab.....                           | 1     |
| 15. Knocked down during altercation.....                      | 1     |

II. *Crushing injuries*.—Three cases, or 14.2 per cent.

|   | Cases |
|---|-------|
| 1. Crushed in freight elevator.....                       | 1     |
| 2. Buried in excavation, crushed by rocks and cement..... | 1     |
| 3. Caught in rising elevator.....                         | 1     |

III. *Direct blow*.—Two cases, or 9.5 per cent.

|   | Cases |
|---|-------|
| 1. Struck on shoulder by iron weight.....     | 1     |
| 2. Struck on shoulder during altercation..... | 1     |

It is obvious that fractured scapulæ usually occur following great violence; also, that the fractures are probably all due to direct force rather than transmitted force through the arm. The history of a fall on the outstretched arm was not elicited in any of this series.

The type of individual, the nature of the trauma, the mechanism, and even the treatment of fractures of the scapula are analogous to that of fractures of the pelvis.<sup>6</sup>

The following two paragraphs will demonstrate the severity and multiplicity of the injuries received and their complications, also the relative unimportance of the fracture of the scapula *per se*.

*Other fractures and dislocations*.—Fractures of the skull, five; nasal bone, one; clavicle, two; ribs: unspecified, one; third rib, two; fourth rib, four; fifth rib, three; sixth rib, two; seventh rib, one; eighth rib, two; ninth rib, one; tenth rib, one; fifth metacarpal, one; transverse process, fourth lumbar vertebra, one; radius, two; ulna, two; dislocation of radio-ulna joint, one; fractures of the ilium, one; ischium, one; separation of the symphysis pubis, one; fractures of the tibia, one; and fibula, two cases.

*Other injuries, diseases, and complications*.—Only four cases had none. The others were: cerebral concussion in ten cases; laceration of the brain,

one; scalp, seven; axilla with hæmorrhage, one; scapular region, one; thumb, one; anal region, one; perineal region, one. There were contusions: multiple, two; of the scalp, one; scapular region, two; shoulder, two; chest, four; back, two; forearm, one; pubic region, two; inguinal region, one; and leg, one. There were also abrasions: multiple, two; scalp, one; face, one; shoulder, one; chest, two; scapular region, one; pubic region, one; and leg, one. Other conditions were: extradural hæmorrhage, one; profound shock, two; ruptured pleura, one; ruptured bladder, one; hæmatoma of the right eye, one; pneumonia, two; conjunctivitis, one; abscess of scapular region, one. It was interesting to note that there were no severe injuries of the soft parts from the fragments of the fractured scapulæ. The one case of the ruptured pleura was due to a fractured rib, not scapula.

The following *symptoms and signs* were present which were attributed to the fractured scapula: local pain in eighteen cases; local tenderness in sixteen; temporary loss of function of the arm was noted in six; temporary partial loss of function of the arm was noted in three. In one case, specific mention was made of the fact that there was no difficulty or pain on motion of the arm, and three were noted to have pain on motion of the arm. No symptoms of any value could be elicited from two of the cases who were unconscious most of the time during their stay in the hospital. Probably due to the multiplicity of the injuries and to the serious condition of most of the patients and the fact that most of them were in shock on admission, the symptoms and signs are very briefly recorded. Scudder<sup>5</sup> mentions the above findings, also crepitus and abnormal mobility in fractures of the body; flattening of the shoulder in fractures of the acromial process, especially if the fracture involves the acromio-clavicular joint; a similarity to dislocation of the head of the humerus and the prominence of the acromion and lengthening of the arm in fractures of the neck. The clinical features of fracture at the neck are referred to by Cotton and Brickley<sup>1</sup> as follows: Position of the shoulder: displacement inward with the shoulder obviously narrower than on the other side, obviously driven in and held in this abnormal position by muscle spasm. Fracture of the neck has been discussed in detail by Hitzrot and Bolling.<sup>3</sup> They stress the point that the old descriptions of the clinical features of fractures in this region are obsolete due to inaccuracy. These original descriptions were made in the days before the X-ray. Some of the cases described as fractures of the scapula were fractures of the humerus. They further stated that fractures of the neck of the scapula may occur in which there is no distinguishable deformity and that there is no displacement that can be affected by raising the arm or by traction. Traction suspension apparatus was evidently not tried.

*Hospital morbidity.*—This refers to the number of days' stay in the hospital: the lowest, one; the highest, forty-two; the average, 14.4 days; and one was treated ambulatorily. The morbidity findings mean nothing as the length of stay in the hospital was almost invariably due to complicating injuries. There were only two cases that did not have complicating injuries.

One of these remained in the hospital for thirty-five days, because of an open operation for removal of a fractured coracoid process; the other was also a coracoid which was treated ambulatorily. Whether a fractured scapula should be treated as a bed case or ambulatorily will be discussed under "Treatment."

The locations of the fractures in this series were as follows: Body, fifteen, or 57.7 per cent.; glenoid, five, or 19.2 per cent.; coracoid process, two; acromion, two; neck, one; and spine, one. It will be noted that this is a well-distributed list, as all of the regions of the scapula are involved.

Displacement of the fragments was noted in eleven of the twenty-six fractures, or 42.3 per cent., the degree of separation varying nearly up to an inch.

There were no compound fractures in this series; four were multiple and two were comminuted.

*Mortality.*—There were three deaths, or 14.3 per cent., all from complicating injuries. These three fatal cases all had fractured skulls.

*Treatment.*—As has been mentioned above, the patients in this series were all bed cases with one exception, the time in bed varying from three to thirty-seven days with an average of about fifteen days. This length of time was due to complicating injuries. The treatment in this series, aside from rest in bed with the patient flat on his back, consisted of a Velpeau bandage in one case, Sayre adhesive dressing in two, immediate sling in one, and sling after ten days in several. In one case the arm was placed in suspension with traction and abduction. This case was so placed following operation for removal of a fractured coracoid process. Open operation was done in only one case. This was the case mentioned above—fracture of the coracoid process and body. Due to separation and rotation of the fractured coracoid process and persistent pain, the coracoid was removed through an anterior incision. The arm was placed in suspension-traction-abduction for eleven days, following which the arm was placed in a sling and physiotherapy given. Pain was relieved but the final functional result was poor. This case was discussed by Dr. Ralph Colp, of our staff, who was inclined to favor conservative treatment in fractured coracoids. Connors also described a fractured coracoid which had been wrongly diagnosed as a fracture of the greater tuberosity of the humerus and treated by immobilization. A good result was obtained in a few weeks by the use of motion and other physiotherapy.

There are several other points brought out in the literature on the treatment of fractures of the scapula which it may be well to discuss here.

*Fracture of the body.*—No mention is made whether these cases should be treated in bed or not. Scudder<sup>5</sup> advises immobilization of the arm by a sling and bandaging the arm to the chest. Longabaugh<sup>4</sup> described a fracture of the lower end of the body in which the rhomboideus major muscle was partly detached, so that on raising the arm the scapula winged outward

instead of being anchored. It was necessary to remove this lower fragment by open operation in order to effect a cure.

*Fracture of the neck.*—Scudder<sup>5</sup> advocates traction-abduction of the arm with the patient in bed. Cotton and Brickley<sup>1</sup> advocate the following method of reduction and treatment: Reduction by leverage of the humerus across the fist in the axilla as a fulcrum; pad in the axilla; arm held at side. Pillow in back between scapulæ and sandbag anteriorly. Fracture board under mattress. Three weeks in bed with hypnotics. Massage after two weeks; motion after three weeks. Hitzrot and Bolling,<sup>3</sup> in reporting eight cases, stated that manipulation or traction had no effect on the lesion and all were abandoned for a Velpeau bandage; also, that massage and baking and careful attention to the after-treatment will give practically perfect functional results, that the resulting function is so satisfactory that ill-advised attempts at correction are to be condemned. Should a type of fracture occur in which the displacement actually promised a bad functional result, the fracture line could be best approached from behind and the glenoid fragment pried into position in this way with correction of the coincident injuries by appropriate methods, (repair of ligaments, *etc.*).

*Fracture of the acromial process.*—Scudder<sup>5</sup> states that there is difficulty in maintaining reduction by any apparatus. He flexes the forearm, lifts the arm upward, and applies counter pressure on the inner fragment, followed by a heavy bandage, and states that union will occur in three to four weeks. Darrach<sup>2</sup> describes a case of an old fracture with non-union; the fragments at operation were found to be joined by a firm band of connective tissue. The band was severed and the bone edges freshened and sutured with silk. There was firm union after four weeks of immobilization. He also tells of a similar case in which Dr. Charles H. Peck placed a Lane plate with an excellent result.

It is difficult to come to any very definite conclusions in regard to the treatment of these fractures and it would be absurd to advocate methods of treatment which we have not tried. In fractures of the body, however, we are able to make some definite recommendations as we have treated a sufficient number of cases and obtained good results. Thus, in the absence of complicating injuries or whenever practicable, the following principles of treatment could be followed in fractures of the body:

*Incomplete.*—Ambulatory, sling, and physiotherapy consisting of heat, massage, active and passive motion every second day beginning after three days and lasting from two to three weeks, after which time sling can be discontinued.

*Complete.*—Whether fragments are displaced or not, flat on back in bed with immobilization of shoulder and arm by a Velpeau bandage. After ten days patient to be allowed out of bed, arm placed in sling, discharged from hospital and given physiotherapy as above for three or four weeks, making a total of about five weeks' treatment.



In fractures of the glenoid, the following suggestions are offered. Bearing in mind that these fractures are into the shoulder-joint, early motion is important unless there is so much separation of fragments as to move the fragments when the arm and shoulder are moved. Thus, if there is great separation, these should be treated by immobilization for three weeks in a Velpeau bandage with the patient in bed followed by sling and physiotherapy, consisting of heat, massage, active and passive motion. If there is not great separation, put the patient to bed with no further immobilization, for three days, and then allow patient to get up, with the arm in a sling, and to be dis-



FIG. 1.—D. P., male, aged thirty-six. This patient fell twenty feet from a scaffold, landing on the shoulder. After admission the patient was unable to move the arm, and there were pain and tenderness in the scapular region. Besides having a fractured scapula, he had contusions and abrasions of the scapular region and cerebral concussion. The above tracing of the X-ray shows a comminuted fracture of the body of the scapula extending into the lower tip of the glenoid, with a separation of over half an inch. This man was kept in the hospital for ten days, during which time the shoulder was immobilized in a Velpeau bandage. At the end of eight days the arm was put in a sling and active and passive motion started. Result good.



FIG. 2.—D. Z., male, aged fifty-five. Fell from a ladder, landing on the shoulder. On admission there were pain and tenderness in the scapular region and pain on motion of the arm. Besides a fracture of the scapula, there were the following injuries: Fracture of the skull, laceration of the scalp, and laceration of the brain. The above X-ray tracing shows a complete fracture, transversely through the body of the scapula, extending into the spine, neck and glenoid, with a separation of about one-half inch. No special treatment was instituted for the fractured scapula. The patient died after three days of the head injury.

charged from the hospital and to receive daily physiotherapy, consisting of heat, massage, active and passive motion.

In fractures of the coracoid process, we have already inferred that conservative treatment is probably advisable.

We can offer no special suggestions in fractures of the neck. We do not know whether displaced fragments could be reduced by manipulation under a general anæsthetic or not. It might be worthwhile trying this for a marked displacement and placing the arm in suspension-traction-abduction and the patient in bed.

We have never tried to reduce a displaced fracture of the acromial

## FRACTURES OF THE SCAPULA

process. It might be advisable to try this by manipulation under general anæsthesia, followed by immobilization of the shoulder and physiotherapy.

*Results.*—The immediate results were recorded as follows: good, in seventeen cases; fair, in one; and three died. Satisfactory follow-ups were obtained in only eight cases, or 38 per cent. Although this percentage is quite low, it is considered fairly good as the majority of these patients were of the foreign laboring type, most of whom have no permanent residence.

*Follow-up.*—(1) Fractured glenoid, crushed inward, in a man who is now sixty-six years of age, seen after three years with perfect anatomical and functional result and no symptoms.

(2) A fractured neck and glenoid with displacement of the fragment laterally into the shoulder-joint in a man who is now forty-three, seen after two and one-half years. He had been doing his regular work as a subway motorman for over two years. Abduction of the arm was found to be  $100^{\circ}$  and forward elevation of the arm  $145^{\circ}$ . This man's legal case had not been entirely settled. Examination gave the impression that the shoulder was muscle-bound and that the settling of the case would tend to improve the function of the shoulder.

(3), (4), and (5) Fractures of the body without separation of the fragments. The first, a man of fifty-two, seen after four years, had an excellent anatomical and functional result; the second, a man of twenty-seven seen after four months, also had an excellent anatomical and functional result; the third, a man of thirty-two, had an excellent anatomical and a functional result of 85 per cent.

(6) Fracture of the acromion and body (see Fig. 3) with one-half inch separation of fragments, a man of twenty-five, who, at the end of three months, had some irregularity of the acromion with moderate limitation of motion of the shoulder.

(7) and (8) Fractures of the coracoid. The first, a man of forty-one, with a separation and rotation of the coracoid, for which operative removal of the coracoid was done by Doctor Colp with a rather poor functional result after about a year; the second, a man of thirty, Doctor Lowry's private case, who had a fractured coracoid with slight displacement, obtained an excellent anatomical and functional result when seen after two and one-half months. Sayre adhesive dressing for one week, followed by sling and motion and other physiotherapy, was used in this case.

The accompanying X-ray tracings (Figs. 1, 2, and 3) show three rather severe cases of fractured scapulæ with separation of the fragments.



FIG. 3.—M. O., male, aged twenty-five. Fell four stories from a scaffold after a brick had fallen on his head. On admission the patient was unable to raise the arm and had pain and tenderness in the scapular region. Besides the fractured scapula, there were the following injuries: Fracture of the skull, cerebral concussion, laceration of the scalp, abrasions of the face and contusion of the shoulder. The above X-ray tracing demonstrates a complete fracture of the acromion with separation of about half an inch, also a fracture of the body just above the spine. The patient was kept in the hospital in bed for twenty-two days because of his other injuries. He received physiotherapy, *i.e.*, massage, active and passive motion of the arm and shoulder, but no further treatment for the fractured scapula. The hospital result was considered only fair. The final result was also fair as a three months' follow-up showed some irregularity of the acromion and some limitation of motion of the shoulder.

CONCLUSIONS

1. Fractures of the scapula usually follow great violence.
2. They are usually associated with other injuries.
3. The associated injuries often interfere with any definite plan of treatment for the fractured scapula.
4. Most cases are treated by closed methods.
5. The staff of the Beekman Street Hospital have treated only one case in the past four years by open operation, and that unsuccessfully.
6. It may seem reactionary to outline any definite methods of treatment, as we have already stated in conclusion No. 3 that the associated injuries often interfere with any definite plan of treatment for the scapula; however, it will be well to have some more or less definite principles to bear in mind in order to avoid a too summary treatment of the fractured scapula just because the patient happens to have other more serious injuries.

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# CALCIFICATION IN CALLUS FORMATION AND FRACTURE REPAIR

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OSSIFICATION is a local transformation of fibrous tissue into solid bone, the constituents of which are derived from the blood. The mechanism of this local chemical change is not understood and so the problems of normal and pathological calcification have been approached essentially from the systemic standpoint. Obviously, such a procedure limits our understanding of chemical bone pathology. We have seen cases of obvious rickets as well as delayed bone union resist the systemic treatment and so we have initiated some studies on the local chemical processes involved in calcification. A study of the mechanism of the repair of fracture offers another approach to a possible solution of a variety of orthopædic problems which are definitely non-systemic in etiology. Though the formation of callus is not a phenomenon *sui generis* and is a resultant of several factors favoring osteogenesis, it nevertheless offers an experimental method for the evaluation of the nature of the local pathology involved in delayed bone union. This paper is concerned with the relation of callus formation to calcification.

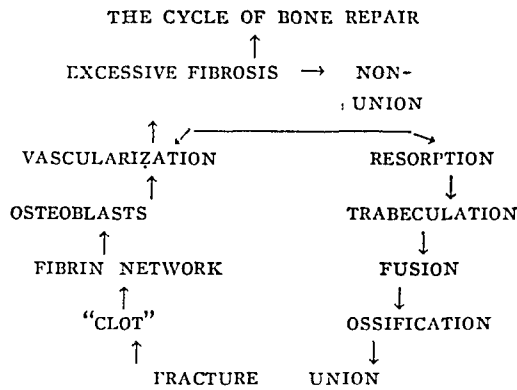
*The Mechanism of Bone Repair.*—The site of fracture following trauma consists of a blood-clot infiltrating the surrounding tissues. The retraction of the fibrin results in a network around the fragments which rapidly becomes invaded by fibroblasts in several hours. This is followed by a metamorphosis of the fibroblasts into osteoblasts with the formation of a soft or fibrous callus. This connective tissue organization of the clot is accompanied by the formation of penetrating capillary vessels.

The vascularization is a vasomotor reaction following fracture, thus bringing about a softening and resorption of the bone ends, a process preparatory for normal bone union. Any interference with these stages preliminary to osteogenesis alters the ultimate formation of solid callus. Trabeculae of young bone tissue begin to appear between the periosteum and diaphysis adjacent to the bone in the organized clot, thereby gradually producing bone union.

The bone in its early stages is coarse, soft, and of slighter density than in its adult stages. If too great an amount of fibrous tissue is laid down in the course of callus formation, the tendency is toward non-union and very often in the soft callus or cartilage stage one will be surprised to find a large, diffuse, palpable callus without any apparent calcification as revealed by X-ray. The fracture will feel fairly firm and solid yet one is never justified in concluding that bone union has taken place.

In certain cases re-fracture takes place, either accidentally or during manipulations to improve position, and it appears that new callus is formed with great rapidity. This is due to the fact that the local changes necessary for this function have already been instituted and it is only necessary to initiate the finer changes.

In the light of the local pathology following trauma, a fractured bone is repaired because of hæmorrhage of the soft parts of the actual break in bone and of the paralytic vasodilation. The hæmorrhage results in clot formation. Embryonic connective tissue appears. The vasodilation produces œdema in the soft tissues and resorption of the fractured ends of bone. The calcium salts thus made available locally are absorbed by the fibrin network which with gradually increasing density gives rise to bone.



*The Nature of Delayed Union.*—Delayed and ununited fractures have a common cause, the difference being a matter of degree. The time required for union varies in the different bones but so long as union is progressing the fracture is regarded as delayed. When organization of the exudate about the fragments is reached so that further osteogenesis is impossible non-union is inevitable. The causes are local rather than constitutional, proved by the fact that local treatment is effective in inducing union in most cases.

|                              |  |
|------------------------------|--|
| Systemic Causes of Non-union | <div style="display: inline-block; vertical-align: middle;"> <div style="font-size: 3em; vertical-align: middle; margin-right: 5px;">{</div> <div style="display: inline-block; vertical-align: middle;"> <div>(1) Focal infection.</div> <div>(2) Thyroid disease.</div> <div>(3) Multiple fractures.</div> <div>(4) Debility.</div> </div> </div>  |
| Local Causes of Non-union    | <div style="display: inline-block; vertical-align: middle;"> <div style="font-size: 3em; vertical-align: middle; margin-right: 5px;">{</div> <div style="display: inline-block; vertical-align: middle;"> <div>(1) Inadequate reduction.</div> <div>(2) Inadequate fixation.</div> <div>(3) Circulatory interference.</div> <div>(4) Interposition of muscle.</div> <div>(5) Repeated reduction.</div> </div> </div> |

In non-union, condensation of callus takes place upon the ends of the fragments with failure to bridge the defect with solid bone. The callus upon the proximal fragment is usually in excess of that upon the distal end, resulting in the formation of nodular prominence on the proximal fragment with a cavity into which the distal fragment articulates. On the other hand,

there may be no reaction of the bone to form callus with resulting atrophy of the fragments.

Delayed union of bones may be due to either mechanical or to chemical causes. Obviously a variety of conditions may prevent union. The fragments may not be in apposition. There may be inadequate fixation or reduction. Frequently the process is actually interfered with by repeated examinations and finally there may be actual injury to the local blood supply preventing the continuous availability of blood constituents necessary for repair.

Chemical causes locally may be productive of delayed union. Tissue injury at the site of fracture results in hæmorrhage. Decomposition of the hæmatoma yields amino-acid, which decalcifies the bone ends (Henderson). The blood phosphates are made available for bone formation by a hydrolyzing enzyme present in the ossifying cartilage (Robinson). A marked increase in the local hydrogen-ion concentration tends to decrease the effective enzyme activity.

Constitutional treatment for delayed and ununited fractures is of no avail once non-union is imminent. The problem is local, confined to the site of fracture. Attempts at increasing the calcium and phosphorus concentrations of the blood by antirachitic measures have failed to show any effect upon the local condition. The stimulation of callus formation has been attempted by Bier's hyperæmia maceration of the fragments under anæsthesia, injection of blood, iodine, osmic acid, calcium salts, phosphates, into the point of fracture. And finally, functional use of the fractured extremity, surgical fixation or bone grafts.

*Experimental Procedure.*—Three groups of rabbits in two separate sets of experiments were studied for the degree and rate of callus formation and calcification. Each rabbit was anæsthetized with ether, blood taken from the heart for chemical analyses and the tibia fractured in mid-shaft. The fracture was immediately put into a plaster-of-Paris case and as soon as this had hardened sufficiently a fenestration was made to allow the introduction of the solution used. These preparations were introduced aseptically through the fenestration directly into the site of fracture. Some of the animals were maintained on the regular diet of hay, oats and leafy greens and the others were put on a special diet. The first group of animals was injected with five cubic centimetres of a 1 per cent. solution of trypsin buffered at 37° C. in the following solution pH 7.4 consisting of 100 cubic centimetres each of:

|                                 |                  |
|---------------------------------|------------------|
| NaHCO <sub>3</sub>              | 0.03 per cent.   |
| NaCl                            | N/10.            |
| MgSO                            | 0.0016 per cent. |
| K <sub>2</sub> HPO <sub>4</sub> | 0.009 per cent.  |

The injections were given at twenty-four- to thirty-six-hour intervals; a long needle was used, being introduced about an inch above the fractured site in healthy tissue so as to preclude as far as possible the danger of infection. The second group of rabbits was treated in exactly the same method with the exception that a tissue extract (fibrinogen) was substituted for the trypsin, one cubic centimetre of the sterile solution being injected immediately upon fracture into the hæmatoma. The third group constituted the control.

These animals were subjected to the same treatment except that no solutions were injected into the site of fracture. The animals were watched carefully for evidence of vascular disturbance which might arise from too snugly fitting plaster bandaging, and in case this occurred new bandages were immediately applied. All animals were X-rayed each week to furnish a basis of comparison in the amount of callus thrown down. Specimens were removed from the animals killed at two- and four-week intervals. These were decalcified *in toto* in a 5 per cent. nitric acid. Longitudinal sections were then made with a very sharp blade for photographs and measurements of the callus. Microscopic sections were finally made from the centre of the callus.

*Discussion.*—Experimentally induced fractures in animals revealed that, all other conditions remaining constant, the amount of available fibrous



FIG. 1.—“Trypsin” series. First and fourth week. (Slight bony union.)

tissue is directly proportional to the degree and rate of calcification. The dissolution of the fibrous tissue normally formed following fracture, by means of an alkaline trypsin solution, diminished both the quantity and rate of bone formation during the course of bone repair. On the other hand, the local injection, at the site of the fracture, of tissue fibrinogen which in itself contributed to the available fibrous tissue content and simultaneously stimulated the fibrous tissue production, increased both the amount and rate of bone formation. Attempts to alter the local fibrous tissue production by means of high protein diet were ineffective in comparison with results obtained by controls. Histological studies revealed similar results. This

## CALCIFICATION IN FRACTURE REPAIR

study indicates that the mechanism of bone repair may be altered by the local introduction of substances involved in the process and vary strikingly in comparison with the indefinite results obtained by attempted systemic therapy.

Bone repair involves: (1) the proximation of the fractured ends; (2) their initial union with the network of fibrous tissue; (3) the transformation of this fibrous network by solid calcium salts. Obviously, any interposition of muscle or fascia between the fractured ends of bone will prevent the formation of the fibrous network. Local alterations in tissue may diminish the available production of fibrous tissue and hence result in a fibrous network inadequate to span the fractured ends. Finally, any injury



FIG. 2—"Fibrinogen" series. First and fourth week. (Solid bony union.)

to the circulation will decrease the available supply of blood constituents necessary for the formation of bone tissue.

The trauma which caused the fracture simultaneously produces hæmorrhage. The blood enmeshed in the fractured ends forms the clot of fibrin. Injury to the periosteum favors additional fibrous tissue formation in this network. There is a definite relation between the mechanism of blood coagulation and this subsequent stage of calcification. Freshly formed fibrin has a greater adsorption capacity for calcium salts; hence, the more fibrin or fibrous tissue available, the more rapid will be the bond of union between the two fractured ends. The initial supply of calcium salts available for



adsorption by fibrinogen is obtained by local amino-acid formation which dissolves at least 20 per cent. of the exposed bone ends. The subsequent and continuous supply of calcium salts is obtained from the blood. The spontaneous healing of fractures thus depends upon the local hæmorrhage induced by tissue trauma. There is no providential protection of the unity of the skeletal structure—unless the conditions are favorable, healing will not take place.

Chemical determination of the blood constituents involved in the calcification process revealed certain alterations in the content according to the



FIG 3—"Control" series First and fourth week. (Good bony union)

local conditions of the fracture and its treatment. The control series of animals showed that the normal course of fracture repair involves an increase in the calcium level of the blood with a decrease in the phosphorus content. The bone repair therefore appears to be a process of phosphorization rather than of calcification. The injection of tissue fibrinogen at the site of the fracture tended to increase the blood calcium with the simultaneous decrease in the controls. This difference in blood effect produced by the introduction of tissue fibrinogen is explicable on the basis of the relative rates of bone repair. It has been repeatedly shown that the protein content of the blood is related to the total calcium injection. Half of the protein concentration is bonded to blood proteins as calcium proteinate. Fluctuations of the blood

# CALCIFICATION IN FRACTURE REPAIR

calcium with variations in total protein of the blood have been observed in nephritis and other diseases where the protein metabolism is altered. A high-protein diet favors an elevated blood-calcium level, particularly if the blood-calcium level is below normal. The high-protein diet maintained a higher calcium level than the controls but all were well within the normal range. Protein injected in the form of tissue fibrinogen injected locally showed a similar trend. Diminution of other blood constituents involved directly or indirectly in the process of blood calcification revealed no change with alterations in the treatment of experimentally induced fractures.



FIG. 4.—“Dietary” series. First and fourth week. (Beginning bony union.)

|         |           |            |           |           |
|---------|-----------|------------|-----------|-----------|
| Mg. Ca. | Mg. Phos. | Mg. Fibrin | Alb.      | Glob.     |
| 100 cc. | 100 cc.   | 1 cc. pl.  | per cent. | per cent. |

## INITIAL BLOOD DETERMINATION FIRST SERIES

|                           |      |     |     |     |     |
|---------------------------|------|-----|-----|-----|-----|
| (1) Trypsin group         | 13.0 | 5.6 | .12 | 5.1 | 1.4 |
| (2) Control group         | 13.0 | 7.8 | .14 | 5.3 | 1.5 |
| (3) Manipulated fractures | 13.0 | 7.9 | .14 | 4.1 | 3.6 |

## FINAL BLOOD DETERMINATION SECOND SERIES

|                      |      |      |     |     |     |
|----------------------|------|------|-----|-----|-----|
| (1) Trypsin group    | 13.1 | 5.5  | .61 | 4.8 | 2.6 |
| (2) Fibrinogen group | qns. | qns. | .33 | 3.9 | .67 |
| (3) Control group    | 9.7  | 5.4  | .39 | 3.7 | 2.7 |
| (4) Diet group       | 14.3 | 6.7  | .25 | 4.2 | 3.3 |

## Blood of May 2

### SECOND SERIES

|                      |     |     |     |     |     |
|----------------------|-----|-----|-----|-----|-----|
| (1) Trypsin group    | 13. | 4.1 | .28 | 4.0 | 3.2 |
| (2) Fibrinogen group | 14. | 3.5 | .83 | 4.0 | 3.4 |
| (3) Control group    | 12. | 3.5 | .24 | 3.7 | 3.7 |

# BERG AND KUGELMASS

## *Blood of May 7*

### THIRD SERIES

|                      |     |     |     |     |     |
|----------------------|-----|-----|-----|-----|-----|
| (1) Trypsin group    | 14. | 3.6 | .23 | 4.1 | 2.4 |
| (2) Fibrinogen group | 14. | 3.8 | .56 | 4.0 | 2.5 |

### THIRD EXPERIMENTAL SERIES

#### BLOOD DETERMINATIONS FROM TIME OF FRACTURE TO TIME OF UNION

#### *Blood of April 11*

|                  | Rabbit | Ca.  | Phos. | Fib. | Alb. | Glob. |
|------------------|--------|------|-------|------|------|-------|
| Trypsin group    | 1      | 14.5 | 6.61  | .379 | 4.43 | 3.34  |
|                  | 2      | 13.2 | 5.99  | .465 | 4.34 | 1.78  |
|                  | 5      | 14.8 | 5.37  | .253 | 4.21 | 1.41  |
|                  | 6      | 13.8 | 7.40  | .512 | 4.70 | 1.13  |
| Fibrinogen group | 7      | 14.4 | 7.00  | .288 | 4.34 | .57   |
|                  | 8      | 9.8  | 9.52  | .338 | 4.29 | 1.66  |
|                  | 9      | 8.0  | qns.  | .669 | 4.83 | 2.59  |
|                  | 10     | 14.2 | 4.31  | .425 | 4.54 | 2.21  |

#### *Blood of May 2*

|                  |    |      |      |      |      |      |
|------------------|----|------|------|------|------|------|
| Trypsin group    | 1  | 12.8 | 3.37 | .219 | 4.50 | 2.87 |
|                  | 2  | 13.8 | 3.73 | .208 | 4.47 | 1.79 |
|                  | 5  | 15.2 | 4.16 | .277 | 3.47 | 2.87 |
|                  | 6  | 14.8 | 3.51 | .221 | 4.21 | 2.31 |
| Fibrinogen group | 7  | 14.4 | 3.75 | .487 | 4.70 | 2.12 |
|                  | 9  | 14.4 | 3.93 | .618 | 3.40 | 3.09 |
|                  | 10 | 14.4 | 3.77 | .575 | 4.05 | 2.41 |

#### *Blood of May 13*

|                  |    |      |      |      |      |      |
|------------------|----|------|------|------|------|------|
| Trypsin group    | 1  | 14.1 | 4.00 | .305 | 3.92 | 3.07 |
|                  | 2  | 13.8 | 4.50 | .221 | 4.17 | 2.72 |
|                  | 5  | 16.8 | 3.80 | .229 | qns. | ..   |
| Fibrinogen group | 9  | 16.0 | 3.75 | .465 | 4.15 | 2.46 |
|                  | 10 | 14.6 | 3.84 | .508 | 3.90 | 2.34 |

### CONCLUSIONS

1. The relation between callus formation and the amount and rate of calcification was studied in rabbits with experimentally induced fractures.
2. The greater the local fibrous-tissue formation, the greater the amount and degree of calcification, all other conditions remaining the same.
3. The blood calcium tends to be higher and the phosphate lower in the course of normal bone repair and the more rapid the rate of calcification the more marked is this alteration in the calcium and phosphate content of the blood.
4. Injection at the site of fracture of alkaline trypsin solution to produce fibrous dissolution markedly retarded bony union in comparison with the control series.
5. Injection at the site of fracture of tissue fibrinogen solution to stimulate increased callus formation markedly accelerated bony union in comparison with the control series.

# SURGICAL MANAGEMENT OF CRANIAL INJURIES\*

BY JOHN STEWART RODMAN, M.D.

OF PHILADELPHIA, PA.

I HAVE chosen the "Surgical Management of Cranial Injuries" as the subject of this address, first, because there are no general surgeons exempt from the necessity of handling such cases; second, because in spite of the voluminous literature on this subject, there is still no absolute uniformity of opinion as a whole, and third, because it is a subject in which I have been interested for some years. It is not a subject to which I can bring revolutionizing ideas, however, but rather one which I shall consider from the general surgeon's point of view. The neuro-surgeons have added considerably to our knowledge of the many problems presented by head injuries in general. I have drawn freely from the experience and comments of this especially interested group.

Head injuries are at the same time the oldest and newest subject in surgery. Even prehistoric man developed a certain skill in trephining. Just how early the practice of cutting holes in skulls to relieve fractures and to let out evil spirits was followed has not been determined, but Dr. George Duncan, anthropologist, has stated in recent studies of prehistoric disease, medicine and surgery, that such was undoubtedly done "in a great many unrelated places on the earth's surface."

One skull found in Peru showed that some early physician worked feverishly in an attempt to relieve a basal fracture of the skull before death overtook the patient. Indentations, epilepsy, melancholia, headache, and even magic, seemed to have been indications for trephining. Certain it is that some of these prehistoric people lived among their fellows with soft spots on their heads—the bone was cut or scraped out with flint, and later, with metal knives: skulls having been found with as many as five trephine openings. Such skulls have been found, not only in Peru, but in France, Denmark and Algiers.

The earliest records come from Egypt, which show that such trephinings were done there. We also find in the poems of Homer, which may be accepted as dating from about 1000 B.C., allusions to head injuries, as well as to many other parts of the body. Hippocrates, writing on this subject, begins his comments on such injuries by one of the very few inaccurate observations he was guilty of in describing the sutures of the cranium—namely, that the number and position of the sutures varies with the form of the head; that the coronal suture is wanting when there is no anterior protuberance of the skull and that the lambdoid suture is lacking if there is no posterior protuberance. He is the first, however, of whom I have

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\* Annual Oration before the Philadelphia Academy of Surgery for 1930.

found record who has devised a classification of head injuries—a form of amusement to surgeons ever since then.

Hippocrates thus divided fractures of the skull into four classes, (*a*) simple fissure, (*b*) contusions without fracture or depression, (*c*) indentations of the outer table and (*d*) fractures by *contra coup*.

Celsus speaks at some length on the subject of head injuries, quoting from Hippocrates. He seems to have more clearly understood indications for conservative or radical treatment as the particular case might warrant. To distinguish a fissure from a suture, he advises the pouring of ink on the part and then scraping the bone; if there is a fissure, the ink will mark it. All depressed bone is to be removed, but no more is to be taken away than is absolutely necessary. He would delay operating otherwise unless dangerous symptoms arise—for at least five days. Galen believed that depressed bone should be removed, but that fissures do not require operation. Paulus seems to have followed Galen, so that Greek and Roman methods of that early day did not differ, in some respects at least, from the conservative attitude toward operation of the majority of this time.

Like surgery in general, no real advance in the management of head injuries was made during the early centuries following the Christian era. Many references may be found referring to this subject, however, amply proving the interest which brain injury has always aroused, as well as the frequency of such injuries long before the motor car of today was dreamed of.

Head injuries have always been a large part of the army surgeon's concern. Thus, in the thirteenth century, Roland, of Parma, wrote a book on the subject, dealing largely with fractures of the skull and wounds of the head, for this period followed closely on the age of chivalry. Then knights in full armor carried on war and their weapons were the lance, mace and battle axe. These warriors were always mounted, and the head was the part aimed at. Roland's knowledge of the important clinical signs of various types of head injury was considerable, and his observations at times would do justice to a well-informed surgeon of today. Thus, he states that fractures of the skull may occur with or without a wound of the scalp, but that the important matter is the injury which has involved the brain or its immediate coverings. This thought has been repeated many times since the thirteenth century, but how many today still think of a given case as having died of a fracture of the skull! Roland went so far as to attempt to differentiate between injuries to the *dura* and to the *pia*. In injury to the *dura*, he states that there is pain in the head, redness of the face, inflammation of the eye, wanderings of the mind and blackness of the tongue. When the *pia* is injured, he thought there was loss of consciousness, loss of voice, pustules on the face, and, if the injury is severe, rigor of body which is a certain sign of death.

Ambrose Paré reported in the sixteenth century rather numerous observations of his cases of head injury. For example, one of these patients had

been unconscious fourteen days after having been hit on the head with a cannon ball! This man had vomited blood as well as having bled from the nose, mouth and ears, and also having had convulsive tremors—evidently an instance of fracture of the base of the skull with markedly increased intracranial tension. Paré trephined this patient and in his notes states that while he had operated, “God healed him and today he is still living.” With all of our surgical progress since then, it is still quite an achievement to save a case of this kind, and there are certainly times when I suspect that influences other than ours have played the larger part. In 1559 Paré’s master and friend, Henry II of France, was wounded by a lance blow in a tournament. The King lived eleven days. Surgeons could not find the lance splinters which had penetrated the brain, although they secured the heads of four criminals that had been beheaded, and experimented upon them to try to determine the probable course of the lance splinters. The King evidently died of a subdural hæmorrhage plus infection. Some of Paré’s other reports are most interesting, but we must not let historical data delay us too long from the present day.

That versatile and great surgeon of the eighteenth century, Percival Pott, wrote a monograph on head injuries in 1759. He was an ardent advocate of early operation, and one finds cropping up in his opinions such statements as “the more pressing the symptoms are, the sooner the operation should be performed,—and all other attempts are worse than useless.” Again—“Inflammation of the membrane always requires, and if slight, sometimes yields to large bleeding, gentle purging and a general febrifuge cooling regimes—even though perforation of the cranium should become necessary.” In so far as fracture is concerned, he thought that unless there was a depression, there was no need for operation—that when infection occurred it was due to a “putrifaction” of the dura mater. He further states that fractures of the skull, considered abstractly, are not so dangerous a thing as they are commonly supposed to be. This fact, though stressed one hundred and seventy years ago, has been generally ignored since and until its repeated reiteration in the last few years. Pott advised that all gunshot wounds should be immediately trephined.

Abernethy in the early part of the nineteenth century must have been much interested in head injuries, and I have found the report of cases from his service at St. Bartholomew’s Hospital quite interesting. He seems to have been as much of a conservative as his distinguished predecessor, Pott, was a radical. In beginning his report of cases, he states that while it had been largely the custom of the times, no doubt due to Pott’s teaching, to trephine early, that in his experience “many cases have occurred of late where, even in fractures with depression, the patients have done well without an operation.” He then reports in considerable detail five case histories to prove his point. Repeated bleeding, purging, saline medicines and antimonials were the treatment used in all of these cases—all showing fracture of the skull, some with depression and all with serious coincident brain

injury. These cases all recovered. Abernethy's comments are interesting: "It appears (he states) very clearly from these cases, as well as from a great number of others to be found in books, that a slight degree of pressure does not derange the functions of the brain for a limited time after its application. That it does not do so at first is very obvious, as persons are often perfectly sensible and free from headache and dizziness immediately after the injury. Whether it may not produce such an effect at some remote period is not so easily determined since this cannot be ascertained but by a continued acquaintance with the persons who had received the injuries." He continues, however, by stating that all whom he has had an opportunity of knowing for any length of time after the accident continued as well as before. He quotes Mr. Hill as substantiating this belief. Abernethy must have been fortunate in the cases he "followed up." Certainly it is contrary to the majority opinion of the present day that those who recover from serious brain injury remain entirely free from later trouble. I think it can be said safely that all know of instances of persistent headache, dizziness and even Jacksonian epilepsy occurring as sequellæ, regardless of the type of treatment at the time the injury was received, and immediately thereafter. In fact, the writer recalls hearing that wonderful teacher of a few years ago, John B. Murphy, state he would much rather die than to recover after having been unconscious from brain injury for more than five minutes. While this statement seems somewhat pessimistic, one is never justified in too great optimism that any given case of serious brain injury resulting in unconsciousness will entirely resume a normal life should immediate recovery follow.

Much more could be said on the historical side of this question. Many of the surgically great seem to have written something on the subject of head injuries. One can get a fair estimate, I think, of the practice of the times if the opinions of a few of these be considered as we have done. From Abernethy's time to the dawn of modern brain surgery twenty-five years ago, some progress was made, of course, but not of great moment as it has only been since then and more especially during the past ten years, that surgeons in general have had a better understanding of the underlying pathology of brain injuries. During the century that has elapsed, bleeding has gone and obvious skull injuries have been repaired where possible. Purging, however, has come back now on a more scientific basis. The advent of anæsthesia and asepsis has greatly increased the patient's chances.

There is still, however, and probably always will be, that irreducible minimum of immediately fatal brain injuries because, in spite of the centuries which have elapsed, and a certain increased storing with utilitarian knowledge, the brain is now the same as it was in the pre-Christian era. There is no axiom in surgical pathology more true than the one which states that the higher the degree of specialization of a tissue, the less is its power of regeneration! The tissues of the central nervous system, being the highest

of all, have none. Therefore, if certain vital brain centres are destroyed, life goes with them, and there is no help for such a situation. There is, however, that increasingly large group which fall between the immediately fatal and the trivial. All of the latter will get well, provided complications do not arise, and most of the intervening group should and do, under intelligent, modern management. These patients should not only get well, however, but if an intelligent plan of management is now used, should get well with a reasonable chance of staying well.

It is not easy to say just when the modern management of brain injuries began. A better understanding, at least, of such injuries seems to have gone hand in hand with the growth of modern brain surgery. For much of this progress, therefore, we general surgeons must give the credit to that especially interested group in the last twenty-five years—the neuro-surgeons.

It is perfectly apparent, of course, that one cannot outline clearly the management of an injury unless the underlying pathology of that injury is clearly understood. The difficulty of anyone, therefore, developing a rational plan of treatment of brain injuries during the centuries which have now elapsed, has been that until very recent years, a clear understanding of brain tissue reaction to trauma has not been definitely known. Even now we cannot say just what happens in the mild cases of concussion, since these cases almost invariably get well. My own better understanding of this matter, however, came with the work of Weed and McKibben, who, in the *American Journal of Physiology*, vol. xlviii, 1919, published the result of their experimental work on the alteration of brain bulk. They showed by direct observation of the brain in experimental animals, that hypertonic solutions of saline injected intravenously, certainly reduced the size of the brain, presumably by decreasing the fluid within the cranial chamber while, conversely, hypotonic solutions (water) injected into the veins, increased the size of the brain, presumably by the escape from the vessels of the watery element; further, histological changes within the brain cells were shown to have occurred where the increased tension was unrelieved—as for example, by trephining to allow more room for expansion—but these changes did not occur when such relief had been afforded. Since that time we ceased thinking of these injuries in the time-honored terms of *concussion*, *contusion*, and *compression* of the brain or *fractures* of the skull alone, and have since thought of them much more in the light of intracranial tension. These terms have been retained for clinical diagnosis since it has proven to be impossible to get surgeons in general to think of intracranial tension alone. In our own work, however, the latter was the keynote and gave the indications for proper management—as put forth in a paper on “A Plan of Management of Cranial Injuries Based on a New Grouping of Such Injuries,” read before this Academy in 1924, and published in the *ANNALS OF SURGERY* in April of that year. We began about that time to group our cases for the purpose of proper management into three groups, depending entirely on the presence or absence of increased intracranial tension as follows:



Group 1.—No increase in intracranial tension. Sub-group A.—Inevitably fatal. Sub-group B.—Mild concussion. Group 2.—Moderate increase in intracranial tension. Group 3.—Marked increase in intracranial tension.

I will not repeat now what has been said in that paper except that further experience since then with a much larger group of cases has in no way made me change my mind about the efficacy of the simple plan of handling these cases presented then—on the contrary, reducing this heretofore complicated question to a comparatively simple one has been of the greatest comfort to us and has, I am firmly convinced, definitely added to the success with which these cases have been handled. I do not mean to suggest that any grouping will change in one iota the result in some of these cases receiving serious brain injury at the time of the accident. Such fall into the inevitably fatal class in whom death ensues quickly and who do not last long enough to develop any increased intracranial tension—these die of shock plus probably a complete overwhelming of the medullary centres. In this type of case, treatment is of no avail. We classify all of those cases falling into this “inevitably fatal” sub-group who never recover consciousness—are inevitably markedly shocked—whose temperatures usually remain subnormal, although a rapid rise to hyperpyrexia is seen in some and whose pulse remains rapid and whose blood-pressure remains low. Incidentally, in such patients one can usually find evidence of fracture of the base of the skull on X-ray examination. Often there has been bleeding from the mouth, nose and ears and even the escape of brain tissue. Death ensues within a very few to twenty-four hours after the accident. All one can do is to treat shock. There is no need here to attempt to reduce intracranial tension since, as has been said, these patients do not last long enough to develop it. The literature on this subject has become enormous and as a result many clinical groupings have been proposed. All of them, however, recognize this inevitably fatal type of case for which little or nothing can be done. It would serve no useful purpose were it even possible to do so, to mention here the different ways in which many of those who have been interested in this subject, group their cases. Such groupings have no real value unless a definite plan of management can be built thereon. I do not wish to make any especial plea for the adoption of my own. To me it has been useful because I have been able to outline much more clearly what each case, as it comes along, shall have in the way of treatment. In the mild types of Concussion Group 1, Sub-group B (no increase in intracranial tension) the spinal pressure will be normal, and the clinical picture will be that of mild concussion. All of this type, unless complications ensue, will get well. The underlying pathology of this group must be imagined from what we know of brain tissue reaction to trauma. There is little more than a temporary anæmia, closely akin to ordinary surgical shock—the only difference being a transient loss of consciousness, or dazing, since the anæmia affects the medullary centres—when the anæmia has been recovered from, the blood-vessels will dilate again, and, as a rule,

the mentality will clear and remain so, unless the next step in brain tissue reaction to trauma is taken, namely, œdema. We do not find œdema occurring, however, in appreciable amounts until the case has progressed to Group 2 (moderate increase in intracranial pressure) with a spinal pressure reading of from 10 to 20 millimetres of mercury. These cases will show clinically, marked concussion, or even contusion with an increased period of unconsciousness, slow pulse and raised blood-pressure. If, when consciousness has returned, the patient is restless and lapses readily when undisturbed into sleep, we may fairly surmise that brain tissue has been minutely lacerated and minute hæmorrhage has added itself to the usual compressing force—œdema. In spite of treatment calculated to reduce this increased intracranial tension at times, the case will progress rapidly to Group 3 (marked increase in intracranial pressure) with a spinal pressure reading 20 millimetres or above. These cases will show the clinical picture of compression—unconsciousness lasting for days or even weeks, giving way to coma if the pressure be unrelieved, with a slow pulse later to become fast and weak, and with an elevated blood-pressure falling as the picture progresses toward a fatal termination. There is no need, in addressing this audience, to enlarge further on these separate pictures with which we are all familiar. So closely does the clinical picture fit the spinal-pressure reading, however, that we have given up doing it as a necessary step in the milder cases of concussion for diagnostic reasons.

The surgical management of any uncomplicated case falling into any of these groups is directed solely at relieving intracranial tension where it is increased. Since there is no increase in Group 1, Sub-group B, the simplest plan is called for—rest in bed three or four days, early and free evacuation of the bowels by magnesium sulphate enemas and a limited fluid intake will suffice, the latter two procedures being routinely done more with the idea of forestalling the development of œdema than of reducing it. In those cases falling into Group 2—to these measures will be added an intravenous injection of a 50 per cent. glucose solution (the latter having taken the place of hypertonic saline in our hands and *most others*) and possibly therapeutic spinal puncture, removing sufficient fluid daily to reduce the reading to slightly above normal, 12 millimetres on an average. In our group of uncomplicated cases, falling into Group 2, there was a small mortality. A greater death rate will, of course, be found in Group 3 (marked increase in pressure above 20 millimetres of mercury). To the plan of management already mentioned for Group 2, one must consider the addition of decompression. After having seen a great many cases since the beginning of this work on the above plan, I must confess to being still somewhat in doubt as to the wisdom of ever doing a subtemporal decompression. As a general rule, it will do no good in the cases which fail to respond to the non-operative plan already given—and yet there is the occasional case, progressing slowly toward the terminal stage of compression in spite of the most active non-operative plan that will, I believe, benefit by decompression. I have seen

such benefit a few times, but more often have been disappointed in accomplishing nothing. In such a case, however, no general anæsthetic is necessary and this simple procedure can do no harm. I intend to keep on doing it, though I believe it will only occasionally be thought of as a probable help.

With increasing experience, spinal tap has become with us more of a treatment than a diagnostic procedure. The character of the fluid means much as, of course, bloody fluid can only mean damage beneath the membranes and, naturally, makes the prognosis more grave.

I have referred to the "uncomplicated case" repeatedly. We have considered, in this plan, such frequent accompaniments of head injuries as laceration of the scalp, fractures of the skull, localizable intracranial hæmorrhage as complications in themselves, each with their own operative indication. There is no need to go into the matter further at this time as many papers have already done so, and I take it we are all agreed that such lesions usually call for surgical interference, except in the linear fractures of the vault or base. Again we shall repeat, however, that it is the injury to the brain which matters and to which we must direct our chief attack, and this means combating intracranial tension. I have not quoted most of the splendid original work which has helped in doing this, as those who have done it are well known to us, and have long since received the credit which they so rightly deserve.

These impressions have been based largely on seeing many of the 800 cases which have occurred on the surgical services at the Presbyterian Hospital since 1925. I am greatly indebted to Doctors Jopson, Hodge and Speese for making it possible for me to have done so. While the series does not include those cases seen prior to 1925 at the Presbyterian Hospital, nor those seen on my services at the Bryn Mawr and the Woman's College Hospitals, I felt that it was better for the purposes of this report to consider only this particular group occurring at one hospital since it is of sufficient size to warrant drawing conclusions from.

## SUMMARY

|  |     |
|--|-----|
| Total number of cases studied.....                         | 800 |
| Group I (No increase in intracranial tension)              |     |
| A. Inevitably fatal .....                                  | 36  |
| B. Concussion (mild) .....                                 | 578 |
| Group II (Moderate increase in intracranial tension) ..... | 65  |
| Group III (Marked increase in intracranial tension) .....  | 121 |
| Total .....  | 800 |

Total mortality of series, 60 or 7.5 per cent.

|                   | L.  | D. | Per Cent. |
|-------------------|-----|----|-----------|
| Group I.....      | 604 |    |           |
| Sub group A. .... | 0   | 36 | 100       |
| Sub group B. .... | 574 | 4  | .7        |
| Group II.....     | 65  | 59 | 6         |
|                   |     |    | 9.2       |

# MANAGEMENT OF CRANIAL INJURIES

|   | L.  | D. | Per Cent. |
|---|-----|----|-----------|
| Group III.....121   | 107 | 14 | 11.5      |
| Mortality of those showing serious brain injury (Groups 1A, 2 and 3)..... | 166 | 56 | 25.2      |

(One case in every four in this series died of serious brain injury.)

## CAUSES OF DEATH

### Group I

|  |          |
|--|----------|
| A. Inevitably fatal.....                       | 36 cases |
| (General and cerebral shock—brain laceration.) |          |
| B. Mild concussion .....                       | 4 cases  |
| Pulmonary embolism .....                       | 1        |
| Terminal pneumonia .....                       | 1        |
| Hæmopneumothorax .....                         | 1        |
| Shock (multiple fractures) .....               | 1        |
|  | —        |
|  | 4        |

|  |          |
|--|----------|
| Group II.....  | 6 deaths |
| General and cerebral shock—mild brain laceration....                   | 2        |
| Peritonitis (simultaneous rupture of intestine) .....                  | 1        |
| Diffuse subdural hæmorrhage .....                                      | 1        |
| Chr. alcoholism—terminal pneumonia .....                               | 1        |
| Hæmorrhage into left lateral ventricle and left internal capsule ..... | 1        |
|  | —        |
|  | 6        |

|                                 |           |
|---------------------------------|-----------|
| Group III.....                  | 14 deaths |
| (All died of brain compression) |           |

## APATHETIC THYROIDISM

BY FRANK H. LAHEY, M.D.

OF BOSTON, MASS.

WE HAVE from time to time in the past few years spoken and written of a seldom mentioned and often unappreciated type of hyperthyroidism which we have termed apathetic thyroidism, in contradistinction to the typical hyperthyroidism of the activation type. In a clinic such as ours, where so many patients with thyroid disease are seen, many patients with this type of the disease remain undiagnosed for such long periods of time and when diagnosed are underestimated as to their seriousness because of their lack of activation, that we believe that a discussion of the differences and dangers of the two types may well be of value.

The diagnosis of frank hyperthyroidism of the typical activation type, particularly in the youthful (Fig. 1) is by no means difficult. Likewise the very obvious seriousness of the activation symptoms which characterize it compels a respect for its dangerous possibilities. One cannot see a patient with flushed skin, rapid, pounding heart, full, bounding pulse, rapid, ceaseless movements, high nervous tension, impressive emotional outbursts, and hot, moist skin, all contradicted by marked myasthenia, without being impressed with (1) the certainty of the diagnosis, and (2) the possibility of a fatal outcome upon the addition of any further burden on the increased intensification of the already existent hyperthyroidism. So outstanding are the diagnostic indications and obvious danger signals of activated hyperthyroidism that its diagnosis is rarely overlooked or its seriousness underestimated.

All that is so positive in activated hyperthyroidism, however, is negative in apathetic or non-activated hyperthyroidism. Activated hyperthyroidism is not necessarily limited, but tends to be so, to the middle-aged and youthful. Apathetic thyroidism appears almost entirely in those patients of middle age and past middle age (Figs. 2 and 3). Patients with activation hyperthyroidism tend to have either well-marked exophthalmos or very obvious stare. Those with apathetic thyroidism tend to have no exophthalmos and little, if any, stare.

Patients with the usual type of hyperthyroidism—that is, the activated type—tend to have glands of greater than normal size, although exceptions may occur in either type, while patients with apathetic thyroidism tend to have small, firm glands without striking increase in size.

Patients with thyroidism of the activated type tend to have pulse rates which are high and of full, bounding character. Those with the apathetic type of thyroidism tend to have relatively low pulse rates, varying from 100 to 120, and not characteristically full and bounding in character.

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\* Read before the Southern Surgical Association, December 11, 1930.

Patients with activated thyroidism show apex impulses which are thrusting and forceful in their type, while the apex beats in patients with apathetic thyroidism are not striking, distinctly not forceful, and obviously unimpressive in character.

The general motor activation of activated thyroidism is characterized by the rapidity of the motions and by the ceaselessness and wastefulness of their character. On the other hand, apathetic thyroidism is characterized by



FIG. 1.—Primary active hyperthyroidism. For purposes of comparison only, an activated type of thyroidism is presented. This is the exaggerated type of activation in a child of six with marked exophthalmos, with no weight loss, but with marked myasthenia; a history of hyperthyroidism of irregular course over a period of two years, a basal metabolism of plus sixty, a pulse rate of 128 to 132. A comparison of these two quite definitely different pictures of thyroidism will serve to illustrate how widely separated apathetic thyroidism is from that of the activated type.

very definite repose, reaching in many instances to a definite apathy which leads us to designate it by this term.

Activated thyroidism is characterized by a moist, hot, soft skin. Apathetic thyroidism, by a dry, firm, relatively cool skin.

Basal metabolism rates in activated hyperthyroidism are, as one would expect, usually proportionately high in relation to the degree of activation, +50 to +100, and over, while the basal metabolism in apathetic thyroidism is proportionately low in relation to the non-activation, as would be expected, +40 and downward to +20, and occasionally under.

Patients with activated hyperthyroidism tend to have had the disease shorter periods of time than do those with apathetic thyroidism, and those with the activated type of thyroidism acquire with it a certain indescribable youthfulness of appearance, while those with apathetic thyroidism have their appearance of agedness exaggerated until they seem unduly old for their actual years. This may be in some measure explained by the fact that the skin of patients with activated thyroidism tends not to be pigmented, but



FIG. 2.—Moderate apathetic thyroidism. This patient represents the moderately apathetic type of thyroidism with a quite typical history. She is forty-eight years of age. She has lost 85 pounds since 1915, her present weight being 88 pounds. She has complained of nervousness, weakness and palpitation since 1923. Her basal metabolism rate was plus thirty nine. Her pulse rate during metabolism was 108 to 120. Her blood pressure was 130/80. Note that this patient in contradistinction to activation is in very definite repose. Note the absence of eye signs. Note the absence of any marked thyroid enlargement and note the senile appearance. It is to be noted also, as stated in the text, that the metabolism is not high and that the pulse rate is not high and that the weight loss has been progressive over a number of years.



FIG. 3.—Advanced apathetic type of hyperthyroidism. Goitre for twenty-five years. Weight loss of 52 pounds between 1925 and 1927. Metabolism plus thirty-six twelve days before operation; pulse 80-84; weight 105 pounds. blood pressure 150/0; auricular fibrillation and a large intrathoracic goitre. Note the lack of activation, definite apathy, dry and wrinkled skin.

possesses the live, warm, moist, pinkish flush which characterizes youth, as described above. The skin of patients with apathetic thyroidism, on the contrary, tends to be dry, cool, lifeless, and with the pigmentation which characterizes old age.

We have, unfortunately, had the opportunity to observe the behavior of individuals of both types during the onset of death following fatal reactions

to surgical procedures. Patients with activated hyperthyroidism die in states of distinct over-activation; those with apathetic thyroidism die in states of distinct apathy progressing into coma.

A fatal reaction following a surgical procedure in thyroidism of the activated type is associated with tremendous activation in all of its forms: cardiac (tachycardia up to uncomfortable rates), respiratory (very rapid respirations), motor (requiring restraint) and mental (up to delirium).

Patients with serious and fatal reactions following partial thyroidectomy for apathetic thyroidism go back to their beds and either never awaken from their anæsthetic, or awaken only to sink comfortably, leisurely, without activation, into semi-stupor or to become completely unconscious and die gently with practically none of those awesome activation signs which accompany death with the typical activation thyroidism, as, for example, seen in a young girl with intense exophthalmic goitre.

It is not my purpose to attempt to create another group in thyroid classification. We have all so simplified the classification of thyroid disease in recent years that it is much better understood and hence much better treated, and I do not wish to further complicate it. I do desire, however, to attempt to establish in the minds of physicians the existence of an atypical thyroidism of this type so that they may not overlook it in diagnosis because of its lack of obviousness, and so that they may not underestimate its unobtrusive but definitely certain seriousness.

As relates to its diagnosis, all patients with unexplained weight loss, unexplained tachycardia, unexplained myasthenia, should be investigated by careful clinical investigation and careful metabolic studies as to the presence of a possible apathetic type of thyroidism, regardless of the absence of any of the typical signs of hyperthyroidism. If physicians will have this atypical apathetic type of thyroidism in mind, we feel sure from our own experience with them that patients whose abnormal states were hitherto not infrequently undiagnosed, will be diagnosed as cases of apathetic thyroidism, submitted to subtotal thyroidectomy, and so be restored to health and relatively normal capacity.

It must, of course, be realized that there exist all gradations between the extremely intense and severe types of activated hyperthyroidism—for example, in a young and active child up to the extreme, almost somnolent type of apathetic thyroidism in an aged person. Fortunately, however, the two types tend to remain, from the very character of their differentiating signs, quite clearly separated, making thus their recognition not difficult when one has in mind the existence of this type of apathetic atypical thyroidism and has had experience with it.

It is very necessary that surgeons who are operating upon patients with thyroidism of this atypical apathetic type should realize the great capacity of patients with this type of thyroidism to die unexpectedly, giving few or no warning signs as to the impending fatality in their course upon the operating table.



Before we recognized and became familiar with hyperthyroidism of this apathetic type, we suffered the unfortunate experience of seeing an occasional unexpected fatality after subtotal thyroidectomy on patients with this condition, in spite of the fact that their course upon the operating table was anything but a disturbing one. Not infrequently patients with apathetic hyperthyroidism will maintain pulse rates upon the operating table during subtotal thyroidectomy of under 120, and without excessive pulse pressure. When these facts are associated in the surgeon's mind with the pre-operative observation that the patient's course pre-operatively has not been an activated one, and his basal metabolism rate has not been high, he is very likely to assume that subtotal thyroidectomy may unhesitatingly and immediately be undertaken with safety. By the same signs and line of reasoning, he is apt to assume, particularly due to the deceptively safe appearing course upon the operating table, that the entire operation can be done safely in one stage. It is in just such cases as this that unexpected fatalities arise. One should look rather to the pre-operative history of the patient and the recognition of the existence of this apathetic type of thyroidism to protect him against too early and too much surgery, rather than those striking danger signals of high pulse rates, high basal rates, high pulse pressure, and recent and excessive activation and intensification of the thyroidism which so characteristically accompany the typical patient with the activated type of hyperthyroidism and warn one of its dangers.

The particular danger signals in the patient with the non-activated type of apathetic thyroidism are marked weight loss, usually gradual and over a long period of time, in contradistinction to the rapid and extreme loss which characterizes activated thyroidism; the existence of the apathetic thyroidism for a long period of time, usually over a year; and an increase in the apathy which characterizes the disease.

We have been so impressed with the possibility of an unexpected fatality in patients with apathetic thyroidism that we have taken the position that the demonstration of the presence of apathetic thyroidism in a patient assumes that some good reason must be advanced why a two-stage operation, right and left thyroidectomy, should not be done. We have assumed the position that all patients with the apathetic type of thyroidism should have right subtotal thyroidectomy, should return home for six weeks, and then return for left subtotal thyroidectomy, with a few exceptions—for the most part patients in whom the disease has not existed for a long time, or there has either been no weight loss or the lost weight has recently been regained. We realize that this will result, in all probability, in some unnecessary two-stage operations, but since apathetic thyroidism carries with it no striking danger signals, but is still capable of serious atypical post-operative thyroid reactions which result fatally, this conservative operative procedure is necessary if we are to overcome the almost trivial operative mortality which still attaches itself to hyperthyroidism, and in our hands is largely related to patients with the apathetic type of thyroidism.

## THERAPEUTIC FAILURES AFTER OPERATION FOR HYPERTHYROIDISM

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EXCISION of a greater or less amount of the diseased thyroid is generally accepted as the best treatment for hyperthyroidism. The most reasonable explanation for the success of this operation (which, by the way, is not uniformly successful) involves an autoactivation and vicious circle hypothesis. The enlarged and overacting thyroid is supposed to produce a secretion which is in excess of the bodily needs, and this excess returns in the circulation to its source and stimulates the gland to continue indefinitely its pernicious activity. The operative reduction in the size of the gland, together with the necessary hæmostasis, cuts off both the excess of secretion and its access through the blood-vessels to the gland.

As the surgeon views his problems, there are three types of hyperthyroidism:

(1) That originating in a simple localized tumor or "toxic adenoma" without other appreciable enlargement of the gland. This group seldom or never presents exophthalmos, has little or no operative hazard, and has an excellent prognosis. But the majority of these patients are later subject to the vicissitudes of abnormal thyroid functionation, as are the other two groups. That is, they are generally of the type called "nervous," and when the organism is subjected to stress or strain the symptoms indicating hyper, or less often hypothyroidism, become manifest. As these patients are familiar with the abnormal sensations, if they recur they generally come back for treatment before any goitre has appeared.

(2) Hyperthyroidism from more than one toxic adenoma. If palpation and inspection show that the gland tissue which intervenes between the tumors is approximately normal in size and consistency, the simple enucleation or excision of the tumors will prove nearly as satisfactory as the enucleation of a single toxic adenoma. But if there is a general enlargement of the gland in addition to the tumor formation, especially if exophthalmos is present (and this is rare), the prognosis becomes less certain.

(3) Hyperthyroidism resulting from a diffuse or general enlargement of the entire gland. In this group, at least in the early stages of the disease, there are no evidences of localized tumor formation. This occurs later. The surgical indications are generally accepted as removal of the enlarged isthmus with resection of enough of each lobe (together with the necessary hæmostasis) to abolish the excess of secretion and still leave sufficient secretory tissue to perform the evidently vital functions of the gland. The most approved, because the least dangerous, technic begins the operation with

division and elevation of the isthmus and attached lobes from the trachea. This obviates the traumatism to the posterior part of the gland which is involved in turning each lobe out by a finger inserted behind it. The prognosis of this group is much less certain than in the other two. In my experience it has a close relationship to the size of the goitre, and the presence or absence of exophthalmos. There is, in addition, to be considered the duration and severity of the hyperthyroidism and its complicating lesions. Exophthalmos occurs in about one out of ten of these cases. Its cause and mechanism are, of course, unknown, but its degree of development seems more or less proportionate to the gravity of the outlook. If the operation proves successful, the exophthalmos seldom disappears before the expiration of two years.

Hyperthyroidism, with a large goitre, on the other hand, as a rule seems to have a better surgical prognosis than that with a small "goitre." Incidentally, the word "goitre" should be restricted to actual pathological conditions of the thyroid, and should not be applied to the simple soft hypertrophy without other symptoms so common in youth and which is apparently an enlargement to compensate for the bodily needs.

These three groups of hyperthyroidism, or (1) the single, and (2) multiple toxic adenoma, and (3) the diffuse hyperplasia of the gland, show a tendency to merge into one another. That is, the thyroid containing a single toxic adenoma may develop one or more other tumors, and at the same time there is usually but not always an enlargement of the intervening glandular tissue. Or the primary diffuse enlargement may have one or more nodules form within it. It is exceptional for the goitre to enlarge after the development of hyperthyroidism. But in the history, the "goitre" is generally the first symptom noted and the hyper syndrome comes afterwards. Occasionally, however, this course of the disease is not apparent, and the hyperthyroidism develops with little or no goitre. This is sometimes actually the case, but more often at least some thyroid enlargement can be detected. This seems to mean that the usual progress of events, or first hypertrophy of the gland, and later its "overactivity," cannot take place. There is some mechanism which should provide for the primary hypertrophy, and this mechanism is lacking in the group of hyperthyroid patients who are the most difficult to cure and who most commonly relapse, or after the usual radical operation develop neuroses which lack the hyperthyroid characteristics. A troublesome anæmia is a not infrequent sequence.

Before citing examples of these observations, it is advantageous to review the little that is known about the physiology of the thyroid. Much can, and should, be inferred from clinical experience. The meaning, for example, of the most common sequence of events, or first hypertrophy of the gland and then hyperthyroidism, should probably be interpreted as a progressive failure in function. Each stage apparently represents an attempt at compensation. There is no doubt that a deficiency of iodine in the ingesta

can cause an enlargement or hypertrophy of the thyroid. This happens, not always but often enough to prove that iodine is an important factor in the change. It is not the only one, because the administration of iodine after the hypertrophy has occurred seldom causes it to disappear. This primary hypertrophy is generally accepted as an automatic attempt at compensation. That is, when the product of the thyroid is inefficient because of a lack of iodine in the alveolar epithelium, these cells multiply and the entire organ enlarges to support their proliferation. This change generally seems sufficient to support the bodily needs for the thyroid product, because in the majority of instances, after the gland reaches a certain size, the hypertrophy ceases and a so-called "simple goitre" persists indefinitely (but may at any time overact). As long, however, as it remains a simple hypertrophy without the development of fibrous or adenomatous tissue, it enlarges by becoming congested whenever the organism requires any increase in the activity of its epithelium. This regularly occurs during menstruation, or during the expenditure of effort which may be voluntary or involuntary, as during an infection or after traumatism or cerebral excitation (nervous strains).

If the primary hypertrophy, which may be due to iodine deficiency, is not adequate for the bodily needs, the next stage in the process should show a more rapid epithelial proliferation, and the infolding of the alveoli, and this change is generally regarded as characteristic of hyperthyroidism. It seems to represent an attempt at compensation which "goes" wrong. The automatic demand for the thyroid product results in an excessive product which is presumably deficient in its iodine content because of the manifest benefit which follows the administration of iodine. The mechanism by which these morphological and physiological changes are brought about is, of course, unknown, but the underlying and general nature of the disturbances seems to me evident.

Where, however, the thyroid enlarges and then overacts without any demonstrable lack of iodine in the ingesta, the process cannot be essentially different. Iodine is still important, as shown by the beneficial effects in hyperthyroidism. But the evidence still points to a primary defect in the quality or quantity of the thyroid product and the hypertrophy (which may not occur) and the later overactivity are in all probability attempts at compensation. In this hypothesis the assumed "weakness" of the thyroid, as shown by its primary hypertrophy and later "overactivity" (when it is not due directly to a lack of iodine in the ingesta), may be congenital as is strongly suggested by the not infrequent familial occurrence of the disease. One should be able to inherit a weak thyroid like a weak brain; a congenital weakness is evident in cretinism, or the weakness might be acquired in many ways. For example, a weakness in organs which, experimentally, support or are functionally associated with the thyroid, like the pituitary or adrenals or others, adds to the complexity of the problem but at the same time shows how the thyroid "weakness" might be acquired. If it can be accepted

that the hyperthyroid gland is primarily a weak and inefficient organ and not one which is viciously overacting and so should be ruthlessly sacrificed, much can be gained. Mutilating operations can at least be avoided, especially in hyperthyroidism with a small rather than a large goitre.

The usual operative procedure is "subtotal thyroidectomy." But this should not be too literally applied, especially when there is little or no goitre. The gland seems to have a marvellous capacity to regenerate, but when it is too much reduced in size it may, and apparently often does, functionally fail. That is, the hyperthyroidism does not cease after operation and the organism continues to show the evidences of thyroid overactivity. The symptoms are not infrequently altered from their original character, but remain distressing and disabling, and are very difficult to relieve. Therefore, the safest operative rule in the presence of a small or absent goitre is to reduce the blood supply as far as possible, and if resection is attempted to make it fulfil the same purpose (reduction of blood supply), and remove only enough of the thyroid tissue to leave the organ approximately normal in size (and this is really a small organ).

The causes which produce the manifestations of the apparent thyroid "weakness" or hypertrophy, and later "overactivity," or overactivity without the preceding hypertrophy, are also debatable, but should not be so obscure when there is considered the accepted and principal treatment of all thyroid abnormalities, namely, rest. Fatigue always intensifies, and rest alleviates the symptoms. Fatigue involves a preceding active metabolism, and the thyroid product is known to be concerned in the metabolism of practically every organ in the body. Infections, or traumatism, or rapid growth, or active cerebration with its reflections upon the viscera through the involuntary nervous system, are among the general causes which should and apparently do originate activity in the general metabolism, and should cause a "weak" thyroid to hypertrophy and eventually to "overact." Hence it is reasonable to regard fatigue in its physiological sense as the ultimate cause of both enlargement of the gland and hyperthyroidism.

As regards "cerebration," or "mental strain," as a cause of the disturbance, it is generally recognized that the "nervous" type of individual is more or less predisposed to the disease. A "nervous" personality is only one which responds to environment with more than the usual expenditure of energy. One who is "nervous" therefore must require active metabolism, and the "weakest" organ in the chain upon which this depends should be the first to fail. In "nervous" men, this seems most frequently to be the stomach, and the result is manifested by gastric hyperacidity and pylorospasm, and later gastric ulcer. "Nervous" women seem more commonly to develop hyperthyroidism. There are many close analogies between these disorders, and not the least is the evident involvement of the involuntary nervous system, and its psychological association with the emotion of fear. In one form or another it is at the bottom of worry, anxiety, excitement or grief which is so commonly present in the history of the origin or beginning of

hyperthyroidism (or pylorospasm and many other neuroses of the involuntary system).

This may or may not have to do with the adrenals and their functional failure with that of the thyroid. However this may be, and whatever part the involuntary nervous system may play in the hyperthyroidism, the surgeon should assume the presence of a weak or inefficient thyroid, no matter how much it may appear to "overact." The gland, therefore, should not be reduced in size beyond that which was the original or healthy normal, and if relapse occurs after operation, unless a reappearance of hypertrophy of the gland is manifest, a secondary radical operation has a dubious outlook. Medical treatment, with rest as its chief ingredient, combined with iodine and organ therapy, and a large admixture of "tincture of time," are more promising.

The following case histories illustrate some of the above observations.

CASE I.—Miss M. L., aged twenty-two, during a strenuous college life noted a slight, right-sided thyroid enlargement (no palpitation). Later after examinations she developed "palpitation" and the pulse rate was found to be 100–120, metabolism plus 20 to plus 30. Goitre just perceptible on the right side. In July, 1919, the right lobe and isthmus of the thyroid were excised with some lessening of the tachycardia, but the asthenia persisted. In November, 1923, there was still inability to do any work. There were insomnia and "shakiness," a pulse rate of 76–140. Metabolism of plus 10. Scar of a "collar" incision. No perceptible "goitre."

During 1923, 1924, 1925, various thyroid preparations were administered, and the best results were finally obtained with a mixture in equal parts of a glycerine extract of thyroid and adrenal. This seemed to gradually relieve the weakness and nervous irritability, and during 1928 she began to perform the duties of a part-time teacher.

In 1929 there was considerable improvement, but she could not endure even a moderate day's work without the aid of the glycerine extract of thyroid. Any other preparation produced tachycardia.

In 1930 there is still persistent the asthenia and nervous irritability. While in bed and at rest, no physical abnormality can be detected. But when up and about "effort tachycardia," with dyspnoea, is evident.

The symptoms all date from the hyperthyroidism which occurred in 1919. Previously, she could be called robust but of a nervous temperament. Hence, it is reasonable to regard the symptoms as due to a defect in what can be called the "driving chemistry" of the nervous system, and the primary cause is evidently a defective thyroid.

This is a typical example of many similar therapeutic failures. They occur most often when the disease develops during adolescence or early youth, apparently, after a combination of strenuous mental and physical effort, and with a small rather than a large "goitre." No matter whether the existing final abnormality is called psychasthenia, or neurasthenia, or neurocirculatory asthenia, it is traceable to the same defect in the nutrition of the nervous system, which in turn is evidently dependent upon a weak thyroid.

CASE II.—J. D., aged thirty-eight, salesman, after strenuous work, developed a small goitre in 1918, but no tachycardia (hypothyroidism).

In 1919 (first operation) the development of exophthalmos, tachycardia and nervous irritability forced operation. The right, or larger, lobe was excised, and after some

improvement during the next month he resumed work. Recurrence of the symptoms followed.

In 1920 (second operation) he submitted to excision of the isthmus and part of the left lobe. After resting three months with considerable gain he returned to work and again relapsed.

October, 1928, typical Graves' disease, with marked exophthalmos. Small, hard remnant of thyroid, apparently the lobus pyramidalis, on right side of thyroid cartilage, and small hard remnant perceptible on left side. Pulse rate 100-120. Metabolism plus 30. Good general nutrition.

November, 1928 (third operation), both inferior thyroid arteries (quite large) tied. Considerable improvement followed. Medication consisted of 1 grain of iodide of iron daily, and 10 minims of a glycerine extract of adrenal. This seemed to control the rather frequent bowel movements. He then attempted to resume work and again relapsed.

March, 1930 (fourth operation), the enlarged remnant of the thyroid on the right side (lobus pyramidalis) was excised. Exploration revealed an apparently posterior remnant of the right lobe. Then the left lobe, about two inches long and an inch thick and very vascular, was resected to leave about the normal amount of tissue. Convalescence was uneventful, and he resumed part-time work after two months of rest. He is now working moderately, but seems dependent upon a 1 grain iodide of iron pill daily, and a mixture in equal parts of glycerine extracts of thyroid and adrenal.

September, 1930, slight exophthalmos. No goitre. Pulse rate 80-120. Metabolism plus 10. Iodine with the glycerine extract of adrenal and a small amount of a glycerine extract of thyroid seem essential to maintain strength enough for even a moderate amount of work.

In each of the operations the goitre could be accurately described as *small*. Benefit followed each resection which at least reduced the size of the gland to such an extent that it was not externally perceptible. It became perceptible only after the resumption of work (compensatory hypertrophy).

CASE III.—Miss N., aged forty, nurse, after a long period of strenuous night duty suffered from extreme fatigue and noted a goitre which was just perceptible (hypothyroidism). Rested and improved, but after another period of strenuous nursing, developed evident but moderate hyperthyroidism.

In 1917 (first operation) both superior vessels were ligated, and the tachycardia subsided. Shortly after resuming work the hyperthyroidism became again manifest.

In 1918 (second operation) the right or larger thyroid lobe was excised and tonsils removed. Complete recovery followed. After three months she resumed work, and the hyperthyroid symptoms again recurred.

In 1925 (third operation) the left lobe of the thyroid, which was just perceptible, was resected. After resting six months she felt well, but on resuming work she again relapsed.

June, 1928, slight exophthalmos, no perceptible goitre, pulse rate 110-120. Weight 120 pounds. Hæmoglobin 40 per cent. metabolism plus 30. Fair general condition. It seemed useless to operate, and she was given a 1 grain iodide of iron pill once daily, and a mixture in equal parts of the glycerine extracts of thyroid and adrenal. A slow improvement followed.

October, 1928, the weight had increased 20 pounds, and the pulse rate varied between 80 and 120, and the hæmoglobin was 60 per cent. She resumed nursing duty but seemed dependent on the combined thyroid and adrenal feeding. Without it she became too weak to work.

December, 1929, came to the hospital after a period of rather strenuous nursing

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work with a fibrillating heart and almost uncountable pulse. Hæmoglobin 30 per cent. Red cells 1,240,000. After two weeks, both the hæmoglobin and red cells had become less and the blood picture showed distinct pernicious anæmia. Lilly's Liver Extract was then added to the thyroid and adrenal feeding, and improvement rather rapidly followed.

September, 1930, hæmoglobin 90 per cent. red cells 4,700,000, pulse rate (irritable) 80-120, systolic blood-pressure 140, weight 132. She is now taking one tubule thrice weekly of the Lilly Extract, and daily the glycerine extracts of thyroid and adrenal, and is again attempting to work and seems normal in health.

CASE IV.—Miss A. N., aged seventeen, has grown nearly 6 inches in the last eighteen months, and during this period developed a "goitre." Menstruation began at twelve years of age, but stopped when the goitre appeared (hypothyroidism?). During the last six months has noted palpitation and recently some exophthalmos (hyper).

December, 1926, very large, well-developed girl (5 feet 10 inches in height), slight exophthalmos, moderate, soft, vascular goitre, neck circumference  $15\frac{1}{4}$  inches, pallid but flushes easily, moist skin, pulse 120-140, weight 170 pounds, metabolism plus 40.

December, 30, 1926.—Novocaine anæsthesia. Both inferior thyroid arteries (very large) tied through a vertical incision behind the lower end of the sternomastoid muscles.

January 7, 1927.—Ethylene anæsthesia. Resection of the thyroid beginning at the isthmus and leaving each lobe a little larger than normal. Histological report of the specimen was "typical of Graves' disease."

March, 1927.—Perfect recovery, except for a perceptible exophthalmos. "Goitre" not visible. Neck  $14\frac{1}{2}$  inches. Pulse rate 76.

November, 1927.—Resumed school work and showed a gradual recurrence of hyperthyroidism.

February, 1928.—Typical Graves' disease again present. Pulse rate 110-120. Goitre enlarging, neck  $15\frac{1}{4}$  inches. Metabolism plus 30. Rest in bed, with 1 grain iodide of iron pill once daily and 10 minims of a glycerine extract of adrenal three times a day, produced marked improvement.

June, 1928.—Again practically normal. But after a rather strenuous social summer relapse occurred.

November, 1928.—Typical Graves' disease again. Considerable but soft goitre, neck  $15\frac{1}{4}$ , pulse rate 120. Five X-ray treatments were administered over the thyroid (combined with rest and iodine and adrenal feeding which previously had been ineffective) produced rapid improvement.

September, 1930.—No evidence of any thyroid abnormality. Goitre has disappeared.

This history shows the effect upon the thyroid of rapid growth and the beneficial influence of X-ray treatment over the gland. In the soft, hyperthyroid goitre, especially when the symptoms are of short duration, this agent is often of remarkable benefit; but the patient must be warned about "overstrain," that is, must be fully aware of so-called "physical limitations," or relapse can be expected. This seems to mean a thyroid which is not competent to promote more than a limited amount of the general metabolism. This does not deny that if the gland is protected or "helped out" for a long enough period it may and probably will become normal.

CASE V.—Miss B. A., aged twenty-three, stenographer. After a period of strenuous work, with little sleep, noted a small goitre (hypothyroidism), and some weeks later was troubled with palpitation and then was aware of "staring" eyes.

April, 1923.—Slight exophthalmos. Easily perceptible small firm goitre, pulse rate 120, weight 109, metabolism plus 30.



Operation consisted in the ligation of all four thyroid vessels, in two stages. This was followed by great improvement, but after resuming work two months later, there was a rather severe tonsillitis and exacerbation of hyperthyroidism. The goitre, which had nearly disappeared, immediately enlarged.

In December, 1923, the tonsils were found "chronically infected." Exophthalmos had recurred. The pulse rate was again 120 and metabolism plus 40.

February, 1924.—Infected tonsils removed. This was followed by an almost immediate improvement in the hyperthyroidism, and after three months of rest the same strenuous mode of life was resumed.

October, 1925.—Reports in apparently perfect health. The exophthalmos and the considerable firm goitre had both entirely disappeared. There had been a gain in weight of 25 pounds.

The most striking feature was the alteration in the structure and functionation of the thyroid. Before the tonsillitis it had only been perceptible; afterward it had become large and showed signs of increasing activity. Then, excision of the spongy, chronically infected tonsils had resulted in a more or less rapid disappearance of all the thyroid symptoms, including the considerable and rather hard goitre. The cause and the effect seem obvious.

Judged from a therapeutic standpoint, the simplest form of hyperthyroidism seems to be that due to a single toxic adenoma. If there is no other gross enlargement of the gland, the enucleation of the tumor will more or less rapidly and without appreciable danger cure the symptoms. But many, if not the majority, of these patients are subject later, under conditions which put stress upon the general metabolism, to the vicissitudes of abnormal thyroid functionation. Hence, many of these patients who present a toxic adenoma seem to have primarily a "weak" gland. The tumor does not usually recur (if one is not overlooked at the primary operation). It can be supposed to originate as a punctate hæmorrhage in the substance of a "weak" gland which has become congested in some attempt at functionation. This smaller or larger hæmorrhage into the substance of the thyroid is not very uncommon, and sometimes causes the sudden development of a painful tumor which is easily (?) differentiable from an abscess. But if the hæmorrhage is minute it might be the focus of irritation around which the proliferating tissues could form an adenoma. However this may be, the gland which appears grossly normal outside of the adenoma should be regarded as "weak" and, therefore, should be disturbed as little as possible. Enlargement of the gland is often apparent with a single toxic adenoma, yet if it is slight, simple enucleation of the tumor is generally curative.

Many of these adenomata show just outside of their capsule a narrow area in which the alveoli have the characteristics of the hyperthyroid gland. Elsewhere these changes are absent, or the alveoli are simply larger than normal. In these cases the post-operative asthenia is generally persistent and can be relieved and convalescence shortened by thyroid feeding preferably with the glycerine extract of thyroid. Only when the toxic adenoma is accompanied by a noticeably diffuse hypertrophy of the gland is it necessary to consider (in addition to the enucleation) resection of the organ.

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Whenever there is doubt, ligation of the accessible vessels is preferable. It conserves presumably valuable tissue.

There may, however, be two forms of the single toxic adenoma, one originating, as suggested above, in a "weak" gland, and another being a truly toxic, benign neoplasm which is analogous to the tumors of the parathyroid or pituitary or adrenal or even of the Islands of Langerhans. Instances of tumors of these organs, with the symptoms of excessive functioning of their characteristic cells, have not infrequently been reported. After excision of the tumor the symptoms disappear. Corresponding tumors of the thyroid should occur. These might be the cause of the "thyroid heart" which of late has been much discussed. These patients usually present a dilated and fibrillating heart with its associated lesions and symptoms, but show very little of the usual hyperthyroid signs, and the metabolism is somewhere near that which should be expected from the heart condition. The clue to the origin of the disturbance can be found in perhaps a small localized tumor in the thyroid. After its excision, which is comparatively simple and safe, the heart and the associated lesions usually return more or less rapidly to normal. May not these true toxic adenomata of the thyroid, when they do not end prematurely in a cardiac death, be the common origin of the carcinomata which are supposed to originate most frequently in a benign tumor of the gland?

The following history illustrates the unrecognized toxic adenoma with serious heart complications:

CASE VI.—Miss B. S., aged fifty-one, teacher, had been ill many years, first with gastric symptoms—for which gastroenterostomy had been performed—then with "heart disease."

In October, 1927, she was emaciated, and though 5 feet 7 inches in height, weighed only 71 pounds. The heart was dilated (apex in the anterior axillary line), very irregular in action, pulse rate uncountable at the wrist. The legs were œdematous. The liver and spleen were slightly enlarged. In the course of the examination, a small tumor, apparently in part calcareous, was found in the right lobe of the thyroid. This, she said, had been present many years. The left lobe and isthmus were imperceptible. It did not seem possible that this partly calcareous thyroid adenoma was the cause of the heart condition, and the treatment was medical for three months. She left the hospital in December, 1927, much improved.

In October, 1928, she returned in a slightly worse condition than the year previously. There was extreme emaciation, diarrhœa and a dilated and fibrillating heart with an uncountable pulse rate. Weight 71 pounds. Metabolism plus 30. After rest in bed for two weeks, under ethylene anæsthesia, the left lobe and isthmus appeared normal. The right lobe, which consisted of an ovoid adenoma about  $1\frac{1}{2}$  inches long and 1 inch thick, was excised. The upper half of the tumor was calcareous, the lower half showed the structure of a "thyroid adenoma." Recovery was uneventful. At the end of a week the heart, with the aid of digitalis, showed a nearly normal action. At the end of a month she left the hospital, and in June, 1929, there was no sign of any abnormality, and there had been a gain in weight of 60 pounds.

It seemed incredible that such a small and partly calcareous adenoma should have caused so much damage, and that the heart could have again become normal.

The following history illustrates a toxic adenoma which occurs in a weak thyroid:

CASE VII.—Mrs. T., aged forty, hard-worked mother of four, had suffered from numerous nasal and tonsillar infections, and finally a vaginal repair and appendix operation. A few weeks afterward she noted a small tumor in the right lobe of the thyroid, and later began to feel tachycardia. There were the usual hyperthyroid signs: a two-inch globular dense tumor in the right thyroid lobe; pulse rate 110–120.

December, 1919.—A cystadenoma was enucleated under novocaine anæsthesia from the right thyroid lobe. The remainder of the gland appeared normal. Recovery within ten days. Pulse rate 76.

October, 1921.—After a strenuous month with sick children returned with complaints of being weak, tired, nervous and wakeful. No goitre. Pulse rate 100.

November, 1921, after two weeks in bed, and 5 minims of a glycerine extract of thyroid three times daily, the pulse rate and general health were normal.

May, 1923, after a strenuous social winter there was headache, nervousness, asthenia and insomnia. No goitre. Pulse rate 80–100. Glycerine extract of thyroid again relieved all the symptoms.

April, 1924.—She sustained a Colles fracture of the right wrist and much pain as proper treatment was unobtainable for three days. After reduction of the fracture and splinting, the thyroid could be palpated for the first time since operation. There were complaints of a "lump in the throat," with headache and asthenia. Pulse rate 80. Glycerine extract of thyroid again relieved all the symptoms, and when the splints were removed the thyroid enlargement had disappeared.

June, 1929, again after a winter of strenuous social life, there were complaints of an aching, "choky" throat, asthenia, headache and insomnia. No goitre. Pulse rate 76. Glycerine extract of thyroid promptly relieved the symptoms.

The following history illustrates a fatal therapeutic failure with multiple toxic adenomata:

CASE VIII.—O. M., aged forty-nine, factory superintendent, first noted a "goitre" as a lump on the right side five years ago after work and worry in the settlement of a strike. During the next two years other nodules appeared, coming after "labor troubles." Then palpitation, sweating, weakness and insomnia followed.

December, 1925.—Physical examination showed good general nutrition, pallor, multiple thyroid adenomata, largest on the right side, scattered throughout both lobes. Pulse rate 90–100. Systolic blood-pressure 140, weight 156. Metabolism was plus 30. After a month of rest, with a 1 grain iodide of iron pill daily, there was no appreciable improvement.

January, 1926, under ethylene anæsthesia, a large substernal adenoma was turned out on the left side and trimmed away, with enucleation of several adjoining nodules and preservation of as much apparently normal tissue as possible. Many adenomatous nodules were then excised from the right lobe. After suture of the remnants of thyroid, and ligation of both superior vessels, each lobe was approximately normal in size. At the close of the operation the general condition seemed excellent, and pulse rate was 80. *Histological report.*—Colloid adenoma of the thyroid.

January 15, or twelve hours later, pulse rate and temperature began to rise, and restlessness and delirium appeared.

January 16, 7 A.M.—Pulse 160, temperature 104°, respiration 40. Delirious. Minims 30 of a non-coagulable aqueous extract of thyroid ("Thyroid Residue") given by hypo every two hours.

January 16, NOON.—Pulse 130, temperature 102°, respiration 30. Delirium less, much improved. Thyroid administration stopped.

January 16, NIGHT.—After 3 P.M., pulse rate and temperature began again to rise, and were not checked by thyroid hypodermatically. Patient died in coma about 6 A.M.

This history of multiple toxic adenomata is reported to show the probable significance of the dangerous or fatal reaction which may follow extensive mutilation of the diseased gland. In this instance the many tumors were scattered over or through tissue which, in the gross, appeared more or less normal and so worthy of retention. The excision or enucleation of the tumors, however, required much traumatism of the apparently sound tissue and, consequently, its function must have been suppressed. The result was a fatal post-operative toxæmia which, at the outset, seemed to be relieved by the subcutaneous administration of a non-coagulable aqueous extract of the thyroid ("Thyroid Residue"). Later this treatment failed. I, as well as others, have reported many instances of the dangerous post-operative "toxæmias" which seem, by the administration of a thyroid extract, to have been saved from impending death. There is at least one report in the literature of a similar success with thyroxin, but I have not dared to use it, chiefly because of its slow effect. The inference to be drawn from these experiences is that the toxæmia is not due to a sudden increase of the "poisonous" (?) thyroid product; the traumatism inflicted upon the secreting cells should suppress and not increase their function. It is more reasonable to believe that the sudden failure of the alveolar epithelium deprives the nervous system of some essential nutritive element and it reacts accordingly. It is probable, therefore, that in advancing hyperthyroidism there is a progressive failure in the nutrition of the central nervous system, and the nerve cells contain no reserves. Consequently, when the inadequate thyroid support is suddenly withdrawn these cells fail. The toxæmia terminates in a coma not unlike that of diabetes. It suggests a nervous starvation rather than a toxæmia. If there were available for hypodermatic use the normal product of the thyroid, the acute thyroid toxæmias could all probably be saved. Thyroxin is undoubtedly a very active derivative of the gland, but experimentally it does not seem to quite fulfil all of the functions of the gland. It acts upon the sympathetic system, and is capable of "sensitizing" it, whatever that may ultimately signify. Aqueous or alcoholic extracts of the entire thyroid, however, seem to stimulate the vagus and, clinically, in early typical hyperthyroidism, the vagus, or parasympathetic system, rather than the sympathetic is most active. It is possible that the advancing thyroid toxæmia is due to an increasing amount of thyroxin in the thyroid product and a decrease in some unknown but vitally important other conjoined material (?).

In these histories a 1 grain iodide of iron pill has been given once daily in conjunction with a glycerine extract of thyroid, or a glycerine extract of adrenal. Sometimes the thyroid and adrenal have been combined. The 1 grain iodide of iron pill (ferrous iodide) of the National Formulary contains approximately 0.8 grains, or 52 milligrams, of iodine. Twenty

minims of the more commonly used Lugol's solution contains about 2.5 grains, or 156 milligrams, of iodine. If this (20 minims of Lugol's solution) is administered constantly in hyperthyroidism, there will be an occasional acute exacerbation of the disease which seems then to mean that the epithelium of the thyroid alveoli is too "weak" to metabolize such an amount of iodine into colloid. For the latter is absent in the toxæmic gland and in its place the alveoli are filled with a mass of disintegrating cells. To be sure, nothing is known about the relationship of the colloid material to the actual product of the thyroid; but the absence of colloid and the presence of severe toxæmia at least suggests that the thyroid is not performing its function. Its normal morphological elements are lacking and, therefore, it is not poisoning the nervous system by functioning too much. If the colloid material represents the secretion of the gland (and there is a general agreement that it does not) the colloid is absent. On the other hand if it is some intermediate product, as seems probable, then the disintegrating cells in the alveoli are manifestly not this intermediate product and the nervous system is "starved."

A toxic adenoma, however, apparently poisons the heart, probably through its nerve supply. But, as in Case VI, the central nervous system is not appreciably affected. It does not show the peculiar irritability of the usual hyperthyroidism.

A 1 grain iodide of iron pill once daily, with its comparatively small iodine content (and about 19 per cent. of iron) seems never to show the occasional dangers of the usual large dose of the compound solution of iodine and is much simpler to "take," and also provides the slightly questionable benefit of the iron. Many of these patients show some anæmia. There are many reports in the literature which show that a very small dose of iodine in hyperthyroidism is as effective as a large dose, and also is preferable.

There is no doubt of the beneficial effects of thyroid feeding in pronounced hypothyroidism, or myxœdema, yet there is no knowledge as to how or where it or any other organ therapy acts. The usual medicament is a desiccated product containing a standardized amount of iodine. Even a minute amount of this material may intensify the symptoms of these "post-operative therapeutic failures" who are afflicted for a long period with asthenia and effort tachycardia. Being convinced that the primary fault in these cases was essentially a hypothyroidism, I have experimented with all the available thyroid preparations, and have found that a glycerine extract (one of the earliest products used in organ therapy) seems the least toxic and the most generally beneficial. It is made by mixing equal parts of glycerine and hashed fresh pig glands. After straining, or filtering, off the coarse particles, 5 minims of the nearly clear liquid contains approximately 0.04 milligrams of iodine. This medication is employed at first in a dosage

## THYROIDECTOMY THERAPEUTIC FAILURES

somewhat smaller than 5 minims, and gradually increased as the tolerance is established.

Several years ago I supervised some experiments which seemed to prove that the feeding of adrenal material increased the iodine content of the dog's thyroid. Adrenalin did not. With this hint, I administered in hyperthyroidism in conjunction with iodine some preparation of the adrenal, preferably a glycerine extract of the entire gland. It seems particularly useful when there is activity of the gastro-intestinal tract, such as abnormal hunger and frequent bowel movements. It is also useful in combination with iodine and a small amount of the glycerine extract of thyroid in the presence of an irritable rather than a constantly fast pulse rate. This represents the common post-operative asthenia with an "effort tachycardia." A glycerine extract of the adrenal prepared like the similar thyroid extract contains approximately 0.14 milligram of adrenalin in 10 minims of liquid. These preparations are available commercially in 5 and 10 minim pills.

During the incipient stages of hyperthyroidism, and especially during the post-operative recovery, many of these patients complain bitterly of a feeling of pressure or constriction in the region of the thyroid. It bears some resemblance to a spasm of the œsophagus, and has in several instances cited in the literature been demonstrated as such (by radiography). For the relief of this symptom, a combination in equal parts of glycerine extracts of thyroid and adrenal is very useful. X-ray treatment of the gland for hyperthyroidism is generally regarded as useless. But in the early stages of a post-operative recurrence it may be curative, as in Case IV. It may also stop the tachycardia in a beginning hyperthyroidism with a small soft goitre. But to be effective it must always be supplemented by preventive and supporting treatment.

### SUMMARY

Hyperthyroidism probably represents an attempt at compensation which "goes wrong." It usually begins with a simple hypertrophy of the gland. The thyroid promotes the metabolism, and so the functional or cellular activity of practically every organ and tissue in the body. It performs this function through an iodized secretion made by the alveolar epithelium. In the hyperthyroid condition of the gland there is a multiplication of these cells. Iodine generally decreases this proliferation, but sometimes increases it. The epithelium thus seems to vary in its vital capacity or ability to metabolize iodine. If the secretion is inefficient from lack of iodine, or from lack of the vital capacity to metabolize it, the gland is "weak" and should hypertrophy to compensate for the bodily needs which are expressed automatically through the blood or nerve supply, or both. These needs are activity in any one or more organs, and the effect is that of fatigue or its biochemical equivalent. The normal response of a "weak" thyroid to promote this production of energy is a multiplication of the alveoli and their

epithelium. If this proves inefficient to meet the bodily demands there is a more rapid proliferation of the epithelium, with a resulting hyperthyroidism. If the normal preliminary hypertrophy is slight or absent this phenomenon should represent an additional unknown factor of "weakness" in the thyroid. Consequently, under these conditions, extreme operative reduction in the size of the gland is of doubtful value.

The purpose of operative interference is to reduce the quantity of secretion and, at the same time, to check the apparent autoactivation of the gland. The latter is the most reasonable explanation of at least some of the effects of thyroid feeding (autoactivation).

The immediately post-operative functioning of the thyroid should be conserved by gentle manipulation of the unexcised portion.

The convalescence, which is often prolonged, needs constant supervision to avoid fatigue, or its physiological equivalent in infection or emotional strain. The thyroid should also be supported by a small amount of iodine to check the epithelial proliferation, and by (experimental) organ therapy to support the "weak" gland; thyroid (when the resting pulse rate is normal) or adrenal (to help the weak alveolar epithelium to metabolize the iodine), or possibly pituitary or ovarian preparations.

# RESULTS OF THYROIDECTOMY

ANALYSIS OF ONE HUNDRED CASES

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FROM THE BUFFALO THYROID CLINIC

THYROIDECTOMY as the best treatment for hyperthyroidism is being challenged in many quarters today<sup>1</sup> and the results claimed for it vary widely, all the way from 18 per cent.<sup>2</sup> to 92 per cent.<sup>3</sup> of cures. Careful and unprejudiced study of the post-operative results, therefore, is needed to clear up this question. Complete pre-operative examination and careful preparation of toxic goitre patients by qualified groups and carrying out of the operative procedure by teams trained in the handling of these cases has reduced the mortality of thyroidectomy to the point where that procedure is no less dangerous to life than medical treatment, radiation, or no treatment at all. The only question that remains, therefore, is which form of treatment offers the best chance of complete and permanent cure.

In this study we have taken 100 consecutive thyroidectomies during the period ending three months ago and compared the pre-operative condition with that found three months later. It is, therefore, a study of the immediate results of thyroidectomy only. We have confined ourselves in this way because our records are almost complete in these cases. It is our intention to follow this group through the coming years and report the final results later. We have taken all thyroidectomies, because the boundary line between non-toxic and slightly toxic goitres is a very indefinite one and to place cases into the one group or the other brings in the personal element. Neither have we separated the toxic adenomas and exophthalmic goitres, because of the confusion that exists regarding their relationship and because most pathological thyroids contain a combination of various histological pictures.

Having thus made the selection of our group entirely impersonal, we have carried out the same principle in our post-operative examinations, using as the basis for our comparisons tests that are not influenced by personal opinion, namely, the pulse, the weight, and the basal metabolism. In addition to these three tests, we have also taken into consideration the patients' own statements as to their nervousness and their general state of health, because even with favorable objective findings, a patient is not cured unless she herself is satisfied and feels good.

Under this latter head would be included most of the subjective symptoms, such as pressure symptoms, shortness of breath, dysphagia, weakness and palpitation.

Taking first the pulse rate, we find that three months after operation



it had decreased in seventy-one, increased in twelve, remained stationary in eleven, with no records in six cases (Fig. 1). The average pulse before operation was  $104\frac{1}{2}$ , three months after operation it was 87. Of those that remained stationary, all were 85 or less before operation. Thus we

|            |    |    |
|------------|----|----|
| DECREASED  |    | 71 |
| INCREASED  | 12 |    |
| STATIONARY | 11 |    |
| NO RECORDS | 6  |    |

FIG. 1.—Pulse three months after operation.

have only 12 per cent. to 13 per cent. that did not show a decreased or a continued normal pulse three months after operation.

A similar condition was found in the weight of these patients (Fig. 2). Sixty-seven patients gained an average of 9 pounds, twenty-one remained stationary, while nine lost an average of 6 pounds (one lost 22 pounds), with no records in three cases. Here again, all who remained stationary

|            |    |    |
|------------|----|----|
| GAINED     |    | 67 |
| STATIONARY | 21 |    |
| LOST       | 9  |    |
| NO RECORDS | 3  |    |

FIG. 2.—Weight three months after operation.

had not lost weight before operation except two. Thus only 11 per cent. did not show a gain, or continued normal weight three months after operation.

A parallel condition was found in the basal metabolic rates (Fig. 3). Sixty-eight patients showed a decreased rate after three months, nine remained stationary, fourteen showed an increased rate, with no records in nine cases. Before operation, the average rate was  $+30$ , the highest being  $+80$ , the lowest  $-23$ . Three months later the average rate was  $+8$ , the

|            |    |  |
|------------|----|--|
| DECREASED  | 68 |  |
| STATIONARY | 9  |  |
| INCREASED  | 14 |  |
| NO RECORDS | 9  |  |

FIG. 3.—Basal metabolism three months after operation.

highest being  $+70$  (see second unimproved case below), the lowest  $-18$ . Again all but one of those who remained stationary had a normal or near-normal rate before operation. We see, then, that only  $15\frac{1}{2}$  per cent. did not show either a decrease or continuance of a normal rate. Incidentally we found the lowest rate after operation only  $-18$ , showing that no serious hypothyroidism followed subtotal thyroidectomy.

Going now to the statements of the patients themselves, first, as to their nervousness, second, as to their general condition, we find the following. Before operation, six patients said they were not nervous, two slightly

## RESULTS OF THYROIDECTOMY

nervous, forty-seven quite nervous, and forty-five very nervous (Fig. 4). Three months after operation, sixteen reported no change, forty-six said

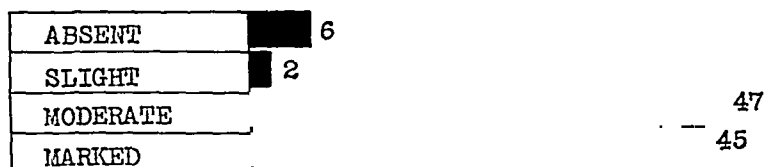


FIG. 4.—Nervousness before operation.

their nervousness was less and twenty-three said that it was much less, with no records of fifteen (Fig. 5). In other words, not a single patient re-

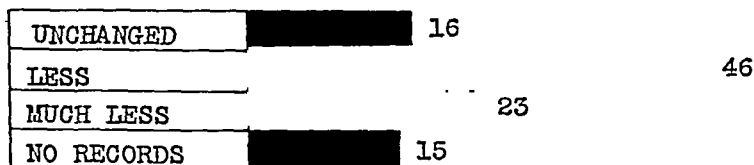


FIG. 5.—Nervousness three months after operation.

ported her nervousness worse, while sixty-nine reported improvement and sixteen no change in three months.

Finally, we have analyzed what the patients themselves think of their condition. While this may not be a strictly accurate way of judging the results of thyroidectomy, nevertheless it is most important. The most complete cure as measured by tests and figures is of little use to the patient if she does not think that she is better. I have divided the patients into

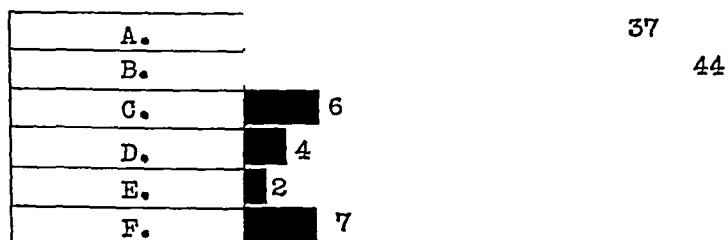


FIG. 6.—General condition three months after operation.

five classes: A, those who report a "perfect result," "feeling fine," "can't find superlatives," etc.; B, those "feeling good," "good recovery," "O.K.," etc.; C, improved; D, very little improvement; E, no improvement. (Fig. 6) shows the number in each of these groups.

Dividing the cases into two groups, those that improved and those with very little or no improvement, we find that 93½ per cent. of those recorded



FIG. 7.—General condition three months after operation.

belong in the former and 6½ per cent. in the latter group, with no records in seven. (Fig. 7.)

An analysis of the six cases that showed very little or no improvement follows:

The first case was the only operative death in the hundred patients, representing 108 operations, 8 having been done in two stages. This patient, a woman of forty, had a very toxic adenomatous goitre and developed a marked post-operative reaction, complicated by a collapse of the trachea, necessitating tracheotomy. Death occurred on the second post-operative day.

The second patient was a woman of sixty with a very toxic adenomatous goitre accompanied by some mental disturbance. Unilateral subtotal thyroidectomy was done, she made a good operative recovery, and was sent home to await improvement before removing the other lobe. There was no improvement, however; she continued to lose weight; her basal metabolism remained at +70; finally she refused to take nourishment, became maniacal, and died about six months after operation.

The third patient was a man of forty-five with a somewhat latent toxic adenomatous goitre. His pulse was 84 and regular, but his basal metabolism was +51 and he had lost 17 pounds in weight. During the operation, his pulse became very rapid and only one lobe was removed. He was sent home and placed on the usual post-operative treatment under the care of his doctor, but at the end of three months he still had a very rapid, irregular pulse and his basal metabolism was +59, although he was feeling better and had gained in weight. We are hoping to get him into a little better condition before removing the other lobe.

The remaining three patients suffered from very toxic exophthalmic goitres. The one, a Polish girl of twenty, had a unilateral thyroidectomy done, but had such a severe reaction that it was considered best to send her home for six months, with definite instructions as to rest, diet, etc., which she promptly proceeded to disregard. On a visit a few days after leaving the hospital, she was found in the midst of a hilarious birthday party.

The second, a young man of eighteen, also of Polish parentage, had a bilateral subtotal thyroidectomy done in two stages and was sent home with similar instructions as in the preceding case. He, too, promptly proceeded to disregard them and inside of one month married, although strongly advised against it.

The third patient, a girl of sixteen, had a bilateral subtotal thyroidectomy done, followed all instructions faithfully, but nevertheless showed only slight improvement at the end of three months. We are hoping that her improvement is merely delayed, as has occurred in a number of our cases not in this series.

Thus we see that of the six unimproved cases, two are probably due to the patients' refusal to coöperate and in two others we are looking forward to later improvement. In all six cases we feel sure that neither medical treatment nor radiation nor a combination of the two would have accomplished any better results, except in the patient who died after operation. She, of course, would have lived a little longer, but in all probability would not have been cured.

Summing up these various findings, we come to the following conclusions:

1. In a series of 100 consecutive thyroidectomies, representing 108 operations, examined three months after operation, 93 per cent. report either satisfactory improvement or complete cure.

2. This percentage is verified to a considerable extent by three objective tests as follows:

- a. An average pulse rate of 104½ before operation was reduced to 87

## RESULTS OF THYROIDECTOMY

after operation and 87 per cent. of the patients showed a reduction or continuation of a normal pulse rate.

*b.* Sixty-seven patients gained an average of 9 pounds, while nine lost an average of 6 pounds after operation and 89 per cent. either gained weight or continued a normal weight.

*c.* An average basal metabolism of  $+28$  before operation was reduced to an average of  $+8$  after operation, while 84 per cent. showed either a reduction or continuance of a normal basal metabolic rate.

3. Taking all factors into consideration, we would place the percentage of cures three months after thyroidectomy somewhere between 80 per cent. and 90 per cent.

4. A study of these cases over a longer period of time may show a recurrence in some, but may also show improvement in some of those that did not improve after three months.

5. With an operative mortality of 1 per cent. and a cure of 80 to 90 per cent. in three months, thyroidectomy seems to offer the best chance of cure in most cases of goitre.

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# BILATERAL EMPYEMA OF THE PLEURAL CAVITIES

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MEDICAL progress since the late war has been remarkable for the triumphs of the thoracic surgeon. Profiting by a rare circumstance which combined the necessity of treating large numbers of severe war wounds of the chest with that of treating even greater numbers of empyemas, he has produced an abundance of excellent work which has revolutionized and radically improved, among other things, the treatment of empyema. His successes are reflected in practice by the more intelligent care of empyema, and in the literature by the appearance of excellent articles upon the subject.

One phase of the subject of empyema, however, has stood apart from the stream of investigation and discussion like some small hamlet untouched amid the changes of a great world. This phase is bilateral empyema. Its occurrence is much less rare than many text-books would indicate. Its severity tends to be exaggerated. Its treatment is sometimes undertaken with a hesitancy that is the complement of unfamiliarity, while the principles of treatment are not always clearly understood. Hence any attempt which may stimulate renewed interest in this subject is not likely to be futile.

Such an attempt has been made here in the form of an outline of the natural history and treatment of the disease based upon forty-one case reports and guided by a review of the literature. The forty-one cases include one case\* personally observed at The New York Hospital and two other unpublished cases† from the same hospital; also thirty-eight cases collected from the literature of the past ten years. The review of the literature briefly summarizes the partial reviews of Scanlan<sup>1</sup> in 1928 and Bozzotti<sup>2</sup> in 1913, and brings up-to-date and abstracts the more thorough monographs of Mackenzie<sup>3</sup> in 1914, Fabrikant<sup>4</sup> in 1911, and Hellin in 1905<sup>5</sup> and 1907.<sup>6</sup>

*Natural History of Bilateral Empyema. Definition.*—The term "bilateral empyema of the pleural cavities" denotes a condition in which pus is found in both pleural cavities at or about the same time.

Bilateral empyema is usually considered a complication of unilateral empyema. It is almost always acute, very rarely chronic.

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\* The author takes pleasure in an expression of his indebtedness to Dr. Eugene H. Pool for a suggestion which inspired this work.

† One of these cases is from the First Surgical (Cornell) Division of The New York Hospital and is included by permission of Dr. James Morley Hitzrot.

## BILATERAL PLEURAL EMPYEMA

*Incidence.*—About 7.7 per cent. of all empyema cases are bilateral according to Hellin<sup>5</sup> who found that 113 of 1,448 empyema cases showed involvement of both sides. Lower figures are usually given. Thus, Lord<sup>7</sup> in Osler's "Modern Medicine" quotes 2.0 per cent., or 5 out of 248 cases; Geitz<sup>8</sup> records 0.8 per cent., or 5 out of 588 cases from a review of twenty-three Swedish hospitals; while my figure is 0.6 per cent., or 3 out of 495 cases at The New York Hospital from 1914 to 1930. Standard text-books, if they mention the subject at all, usually agree with Da Costa<sup>9</sup> in saying "in civil practice I have seldom seen it." Graham,<sup>10</sup> however, observes that empyema "is bilateral in probably less than 5 per cent. of . . . non-fatal cases."

For children, Holt and Howland<sup>11</sup> call empyema "bilateral in about 3 per cent. of all cases, but oftener in infants."

The incidence during the epidemics of influenza of 1917 to 1919 was very high. Dunham<sup>12</sup> found it to be 42 per cent. in the United States Army Camps in 1917, or 253 out of 603 empyemas. Stone's<sup>13</sup> figure was 19 per cent. at Fort Riley for the winter of 1917-1918; he observed 19 out of 100 empyema cases. Likewise with other epidemics of influenza the incidence may be high; thus Mackenzie<sup>3</sup> saw many cases during an epidemic near Portland, Oregon, in 1899.

*Age.*—The average age is eleven and one-half years. Extremes of eight months and sixty years were reported by Fabrikant.<sup>4</sup> About 75 per cent. of cases occur before the twelfth year.

*Sex.*—Males predominate over females by 3 : 2.

*Primary Disease.*—The most frequent cause is pneumonia; it preceded 75 per cent. of cases. Three-quarters of these pneumonias were bronchopneumonias. "Primary" bilateral empyemas accounted for 20 per cent. of Fabrikant's cases.<sup>4</sup> One of the cases of this series might so be classified (Case 26).

The rarer causes are pyæmia, tuberculosis, actinomycosis and the exanthemata. Surgical operation or its complications may also precede. Very interesting is the epidemic of puerperal sepsis which was followed by many cases of bilateral empyema described by Charrier<sup>14</sup> in 1855; the occasional cases recorded since have been collected by Hellin<sup>5</sup> and Fabrikant.<sup>4</sup>

*Bacteriology.*—The pneumococcus is the usual causative organism. It was cultured from the pus of twelve patients of this series. The hæmolytic streptococcus, however, almost invariably accompanied the post-epidemic influenzal cases. A variety of other organisms may be present.

Rarely a different organism is obtained in the two sides, as with Case 39.

*Pathology.*—The pathology does not differ from that of unilateral empyema.

*Pathogenesis.*—The involvement of the two sides rather than one may be accounted for in part by a preceding pneumonia of the two lungs, and this was true of twenty-one cases of this series. An increase of virulence of

the infective organism may also be a factor as was indicated by the high incidence accompanying the wartime influenza epidemic. On the other hand, there are patients whose lowered resistance is a predisposing cause, as illustrated by Cases 40 and 41. Occasionally empyema of both sides follows pneumonia of one lung (Cases 30, 31 and 40). Here the empyema of the other side possibly arose from a pneumonia so slight as to be overlooked, or possibly by metastatic infection. The cases of "primary" empyema are very difficult to explain.

Why should not bilateral pneumonia more often be followed by empyema of both sides? Certainly the majority of the pneumonias of both lungs which are succeeded by empyemas are succeeded by an empyema confined to one side. It may be that most pneumonias mature with unequal rapidity on the two sides so that the antibodies from the first empyema are sufficient to prevent a contralateral empyema.

The time of appearance of the two empyemas may be simultaneous, as shown by Cases 31, 32 and 41; or not, as Cases 33 and 39 illustrate. In Case 33 almost two months intervened.

*Diagnosis.*—Diagnosis presents no unusual features, and it will be correctly made more often if the condition be borne in mind.

*Complications.*—These are similar to those of unilateral empyema.

*Prognosis.*—The mortality was 37 per cent. for Fabrikant's series of 118 cases.<sup>4</sup> It is 19.5 per cent. for this series, but this figure is of little significance as it omits all the numerous deaths of 1917 to 1919.

The prognosis should be influenced greatly by the type of the infection. Thus many patients with the pneumococcic type recover, whereas there is no record of recovery of a single individual with the streptococcus hæmolytic type. Failure to make this distinction may have influenced certain authors, Heuer<sup>15</sup> for example, to classify all bilateral empyema "among the fatal cases of empyema." However, cases following influenza are by no means necessarily fatal. Thus, Mackenzie<sup>3</sup> saw at least three during the Portland epidemic of 1899 (Cases 6, 7 and 8), while Cafritz<sup>16</sup> and Beck<sup>17</sup> successfully treated influenza cases, the latter that of a pregnant woman (Case 25).

*Treatment. (A) General Principles.*—The general principles of the treatment do not differ from those of unilateral empyema, and may be found thoroughly discussed in any of the principal works on chest surgery<sup>18</sup> written since the late war. A brief note on current practice must suffice here.

(a) Maintenance of the nutrition of the patient by high-fluid and calorific intake is very important; for empyema is sometimes like typhoid, a long wearing disease.

(b) Obliteration of the empyema cavities is to be accomplished by drainage and reëxpansion of the lungs. Thoracotomy with rib resection is often necessary, though intercostal drainage alone may suffice. The patient may hasten reëxpansion by using blow bottles. Secondary operations to promote drainage or to prevent chronicity may be required.

The drainage tubes should not be permanently removed until the empyema cavities have become obliterated as shown by physical signs and by röntgenograms, and until discharge from the wound sinuses has become slight in amount and sterile.

Drainage should be deferred if possible until the pus within the pleural cavity has become thick, thoracenteses being employed meanwhile. Thus intrapleural adhesions will have time to form, and the pneumonic process to subside. Streptococcic empyemas must not be drained as early as pneumococcic and other types of empyema.

Rarely, repeated thoracenteses may cure a bilateral empyema.

(c) Avoidance of open pneumothorax is a measure of great importance. It should be attempted by using drainage of the closed type; in other words, by drainage which maintains a negative intrapleural pressure. After some days the closed may be changed to the open type.

(d) Sterilization of the empyema cavity may best be accomplished by frequent irrigations with some solution, such as solution of chlorinated soda (Dakin's). The solution if kept warm will avoid heat loss from the lung.

(B) *Particular Application.*—For discussion, let us assume that there is a patient having bilateral empyema of similar extent and duration on the two sides. Let us further assume that by application of the principles outlined above a decision has been reached that it is time for drainage. The question immediately arises as to whether to drain both sides simultaneously or not.

To this question many writers have in the past answered "No" because of the fear of bilateral open pneumothorax. They have based their fear upon the assumption, prevalent up to the ending of the late war, that an open pneumothorax of both sides would be followed by collapse of both lungs and consequently by death.

Investigations carried on during and since the late war, particularly those of Graham and Bell,<sup>19</sup> have shed new light on the pneumothorax problem and on the treatment of empyema. They have shown that the mediastinum of normal individuals is so flexible that it will readily transmit smaller pressure changes from one pleural cavity to the other; in other words that the chest may be considered practically as one instead of two cavities in so far as intrapleural pressures are concerned.

They have also determined that there is a certain area of opening into the pleural cavity, 51.5 square centimetres, which is the maximum compatible with life if the thorax is normal and if the individual's vital capacity equals 3,700 cubic centimetres (a common average figure for the vital capacity). This is so because of a definite relationship between the amount of air entering the lungs and that entering the pleural cavity. Openings into the pleural cavity smaller than 51.5 square centimetres are increasingly well borne. It is to be understood, however, that the above deductions were made with reference to the normal thorax. If the mediastinum is stabilized



by adhesions or by induration, then a unilateral opening of much larger size than the one mentioned may be made. On the contrary, if no such stabilization has occurred and if the patient's vital capacity is low (*e.g.*, 1,000 cubic centimetres) because of pneumonia, or other reasons, then a much smaller pleural opening may be fatal. Since it is the area of opening and not the number or position of the openings that is of importance, similar openings into each pleural cavity will have no more ill effect than a single opening into one pleural cavity of twice the area.

Experience has justified these theoretical conclusions. Many soldiers with surprisingly large open wounds of both chest cavities survived. Moreover, eleven patients with bilateral empyema<sup>20</sup> have been operated upon by simultaneous thoracotomies on both sides. No patient died as a result of the operation; one patient collapsed temporarily but was resuscitated, and another died twelve days later from a cause not attributable to the operation. Furthermore, forty-two other patients<sup>21</sup> were operated upon by almost simultaneous thoracotomies, that is to say by thoracotomies performed on the two sides within twenty-four hours of each other. None of these patients died, and all eventually recovered. Thus, a total of fifty-three simultaneous, or nearly simultaneous, thoracotomies has been performed without a single operative death, and with eventual recovery of all but one patient.

Bilateral simultaneous thoracotomy for bilateral empyema, then, has proved itself an excellent method of treatment. This will be more apparent when it is observed that all the above simultaneous thoracotomies were performed under the open method, hence under conditions less favorable than would have prevailed under the safer closed method. Certainly simultaneous or nearly simultaneous closed thoracotomies should be more extensively used in future. It is also notable that many patients are very little relieved after the first thoracotomy; they tend to remain very little changed until after the second thoracotomy when they often show sudden and remarkable improvement, as was the experience with Case 39 and others of this series. Delay in opening the second side, therefore, seems to accomplish little, but rather to weaken the powers of resistance; another reason for the simultaneous method.

If for some reason it is decided not to drain simultaneously, there arises the question as to which side is best for the initial operation. The left side has usually been preferred because of the belief that the heart would thereby gain greater freedom of action, and that pericarditis would be less apt to occur. These are worthy considerations. Concerning the likelihood of pericarditis Dunham<sup>22</sup> says that "there is no marked difference in the relations of the pericardium to the pleura on the two sides of the chest, and pericarditis has occurred at least as frequently with an empyema on the right side as with one on the left."

If the empyemas are quite unequal in extent, the larger should be drained

## BILATERAL PLEURAL EMPYEMA

first; but again, let it be repeated that the second side should be drained very soon thereafter. In the interval thoracenteses are usually beneficial.

CASE I.—(Personal observation.) A girl of two years, Jewish, was admitted to The New York Hospital, December 18, 1928. *Family History*.—Three of the ten brothers and sisters were dead before the age of four years of pneumonia, meningitis, and diphtheria. *Previous history*.—One year before admission there had been an operation for abscess of the right thigh, the operation being complicated by pneumonia

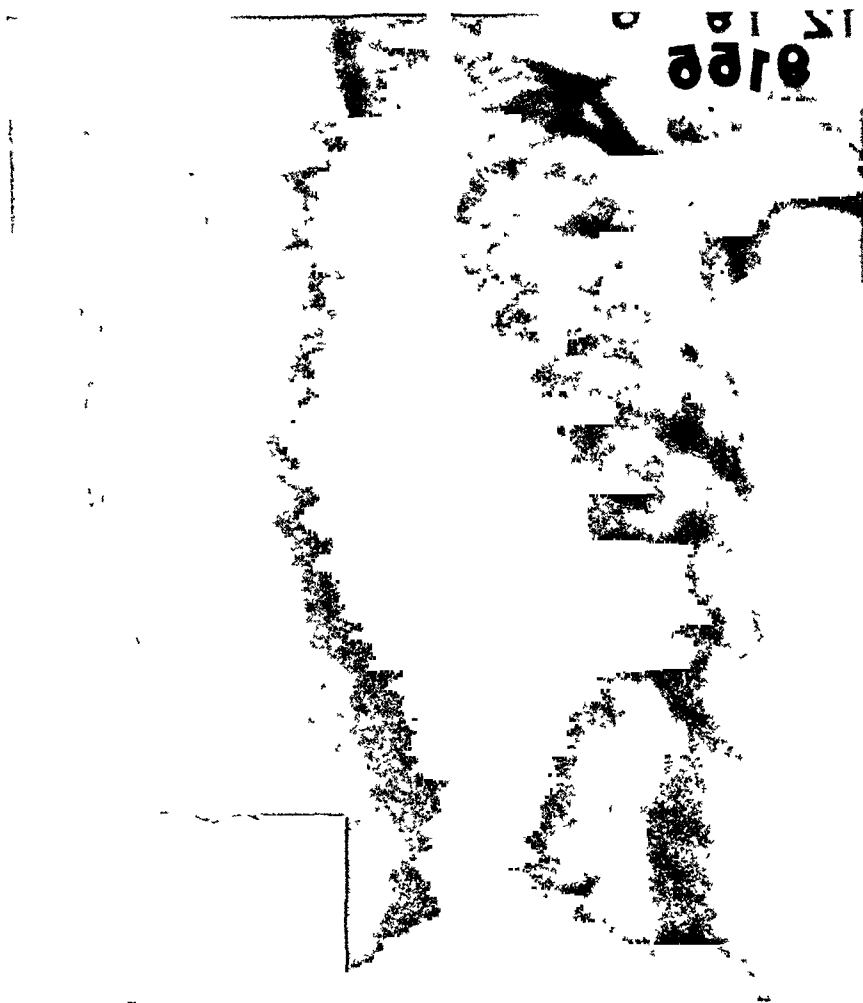


FIG. 1.—Chest roentgenogram of the case observed personally (Case I—Case 41 of table) taken the day after admission, December 19, 1928, showing beginning effusion at the right and possibly the left base and early bronchopneumonia. This report and the three that follow are by the late Dr. Webster W. Belden, of The New York Hospital.

and diphtheria. Thereafter the gait was limping. *Present illness*.—The mother stated that fourteen days previously, December 4, the child had caught cold, and later coughed and had a chill. The family physician found the child to have a high fever, and put her to bed. There was considerable improvement for a week, but thereafter a relapse. The coughing increased, and much thick yellowish material was expectorated. Finally the child became drowsy. *Physical examination*.—On admission the child appeared very sick and emaciated. The temperature was 100.2 degrees Fahrenheit. Respirations were rapid and grunting, and there was a frequent non-productive cough. The chest was symmetrical and equally expansile. Both *lungs* showed dullness posteriorly up to the angle of the scapula; the left axilla also showed dullness. Breath sounds, voice sounds, and fremitus were unchanged from the normal. The *heart* was percussed  $5\frac{1}{2}$  centi-

metres to the left of the midsternal line in the fifth interspace. The pulse rate was 110 to the minute, the rhythm regular. The leucocytes were 12,400 per cubic millimetre with 83 per cent. polymorphonuclear leucocytes and 17 per cent. lymphocytes. The urine was normal, and other findings normal.

A *diagnosis* of bilateral bronchopneumonia and bilateral acute empyema was made. It was confirmed by röntgenogram on December 19 (Fig. 1) which revealed pleural effusion at both bases and bronchopneumonia. Thoracenteses three days after admission (December 21) yielded thick greenish pus from both pleural cavities. *Cultures* from both sides showed a pneumococcus type I. A total of 80 cubic centimetres of pus was withdrawn from the right side, and an amount unrecorded from the left. Seventy cubic centimetres of pus were withdrawn from the left side the next day. Little improvement followed. The child lay propped up in bed, semicomatose and cyanotic, struggling to breathe and to cough. It was now or never for drainage; moreover, six or more days of waiting after onset of the empyema seemed time enough to render opening the pleural cavity relatively safe. It was decided to drain the right side first because of the preponderance of pus in the right chest. Physical signs showed displacement to the left of the heart and trachea, while the signs of fluid extended on the right as high as the spine of the scapula posteriorly, and to the third rib anteriorly in the midclavicular line; whereas on the left they extended only to the angle of the scapula posteriorly, and were absent anteriorly. Meanwhile it was hoped that repeated thoracenteses would take care of the left side.

Accordingly *operation* for closed drainage of the right pleural cavity was performed December 24. With the patient seated the operative field was prepared by application of a half-strength solution of tincture of iodine. A preliminary thoracentesis at the operative site yielded thick pus. After infiltrating the overlying skin with 1 per cent. procaine a small incision was made in the eighth right interspace in the posterior axillary line and carried down to the parietal pleura. A No. 22 French catheter was then seized in a Kelly clamp and plunged through the unopened pleura into the pleural cavity. Thick pus immediately flowed through the catheter which was clamped off in order to maintain closed drainage. The soft tissues and skin were then approximated closely about the catheter by silkworm sutures passed through an encircling cuff. The operation lasted ten minutes and caused no reaction.

With the patient removed to the ward a drainage-irrigation apparatus was arranged. The end of the catheter, which protruded from the wound, was connected by a glass Y-tube to two other tubes, a drainage tube and an irrigation tube. The drainage tube was carried under the bed to a glass receptacle and its end kept under water. The irrigation tube led up to a bottle of irrigating solution hung at the head of the bed, and was kept clamped off except when in use. Before removing the clamp from the catheter which protruded from the wound all the tubing was filled with a solution of chlorinated soda (Dakin's), and all air excluded. After removing the clamp negative pressure was thus immediately exerted on the empyema cavity.

The tubes were irrigated three times a day by allowing to flow through them about 10 cubic centimetres of the solution of chlorinated soda from the bottle at the head of the bed. When clogged by pieces of exudate, as often happened, the apparatus was disconnected, and the protruding catheter irrigated by manual suction with a syringe until all obstructions were removed. During this procedure the protruding catheter was never for a moment left open except while being subjected to negative pressure. Then, after cleaning the apparatus it was reconnected. Responsibility for the apparatus and its proper working rested with one house officer.

The amounts of pus drained day by day varied greatly. No accurate measurements were made, but some days at least 100 cubic centimetres were returned. On one occasion 70 cubic centimetres of pus were withdrawn through a syringe within a few minutes. As a rule manual drainage proved more efficient than mechanical arrangements for the

removal of pus and exudate. Large clumps of whitish-yellow fibrinous matter were often obtained; the pus or exudate bore some resemblance to curdled milk.

Slight improvement in the condition of the patient followed operation. The temperature ranged between 100 and 101 degrees, sometimes reaching 103 degrees. The nutrition remained poor. Fluids were forced. A transfusion of 200 cubic centimetres of whole blood was given (December 26). The left pleural cavity was tapped repeatedly; December 26, forty cubic centimetres of pus were obtained; January 1, forty, and January 3, only eight.

The right pleural cavity was reported free of fluid by a röntgenogram of December 31, seven days post-operatively, but the left chest still showed haziness and mottling.

Closed drainage was replaced by open on the eighth day after operation (January 1). The catheter was removed and a soft open rubber tube put in its place.

The patient's condition was becoming steadily worse. While not so sick as just before the first operation she still did not appear to be very far from death. Examination revealed a rather extensive bronchopneumonia of both sides added to the left empyema. The wound on the right continued to drain moderately.

Since the right lung was well expanded it was decided to open the left side. The twelfth day post-operative, therefore (January 5), *operation* for closed drainage of the left pleural cavity was performed. The technic employed and the after care were similar to that already described.

Immediate and continued improvement followed operation. The temperature gradually subsided to normal. The child was allowed up after the twenty-seventh day post-operative, the temperature never exceeding normal limits thereafter.

The closed drainage of the left side was changed to open on the fourth day post-operative by removal of the catheter and insertion of a soft rubber tube into the wound.

The drainage tubes were retained in both sides until the thirty-third day after the second operation (February 7) when they were finally removed.

Röntgenograms of the chest after the third day following the second operation (January 8 and 16) showed both pleural cavities free of fluid and both lungs completely expanded and clear.

The patient was discharged cured April 4, 1929, about four months after the onset of illness. She had gained much weight and was in excellent physical condition. Both wounds were completely healed. There were no abnormal physical signs in the chest, and no cough.

The condition was entirely satisfactory when seen in the Follow-Up Clinic July 7, 1929.

CASE II.—A boy of seventeen was admitted to The New York Hospital May 18, 1918. The *family history* and *previous history* were irrelevant. *Present illness*.—The patient was taken with pneumonia of the right lung April 29, 1918, which spread to the left lung on May 4. The family physician made a diagnosis of pleurisy of both sides, the right more marked. *Physical examination*.—The day of admission the patient appeared emaciated and acutely sick. The temperature was 102.4 degrees, Fahrenheit, pulse 126, and respirations 34. The right chest lagged during inspiration. The right lung showed flatness below the angle of the scapula with diminished breath sounds; anteriorly there was flatness below the level of the nipple and diminished breath sounds with ægophony and pectoriloquy at the level of the nipple. The left lung showed impairment of percussion, and a few coarse râles below the angle of the scapula. The urine was normal and the examination was otherwise normal. A provisional *diagnosis* of empyema of the right pleural cavity was made.

At operation the next day open drainage of the right pleural cavity was performed. Gas oxygen anæsthesia was employed. A needle was inserted in the eighth interspace, posterior axillary line, and pus obtained. One and one-half inch of the eighth rib was

then resected. After opening the pleura a large empyema cavity was revealed. Two rubber tubes were inserted for drainage. Culture from the pus revealed streptococcus viridans.

Following operation there was moderate improvement. A röntgenogram seven days later (May 26) showed a thickened right pleura and right pneumothorax, but no fluid in the right chest. The wound did not drain well so exploration of the wound was done ten days after the first operation (May 29). Under gas-oxygen anæsthesia a finger was passed into the cavity through the wound, but no pocketing was found. A drainage tube with suction, closed drainage, was applied, and following operation the cavity was regularly irrigated according to Carrel-Dakin technic. The condition then showed slight improvement. Cultures from the wound showed a mixed culture of pneumococcus type II and staphylococcus aureus.

Improvement was such that the patient was up and about from June 18 to June 25. He was then returned to bed because of accumulation of fluid in the left chest as shown by physical signs and röntgenogram.

*Operation* for open drainage of the left pleural cavity was performed fifty-one days after the first operation (July 3). The technic was the same as for the first operation, except that the ninth instead of the eighth rib was resected. Culture from this side showed a pure growth of pneumococcus which was not typed. Rapid improvement followed this operation and the temperature remained within normal limits after the fifth day post-operative.

The patient was discharged in excellent condition July 13. He left against advice, but the right wound had completely healed, and the left was closed and granulating.

A follow-up a year later, July 25, 1919, showed the patient in good health.

CASE III.—A boy of two and three-quarter years was admitted to The New York Hospital September 19, 1917. The *family history* and *previous history* were irrelevant. *Present illness*.—The child was taken with cough and fever September 1. He grew worse and developed severe dyspnœa on September 12. *Physical examination* on admission revealed a very sick white boy coughing frequently. The left lung showed dulness, bronchial breathing, and a few coarse râles below the angle of the scapula posteriorly, and dulness between the third and sixth ribs anteriorly. The right lung was normal. The heart was displaced, slightly, to the right. The leucocytes were 38,600 per cubic millimetre of blood; 86 per cent. were polymorphonuclear leucocytes. The urine was normal, and the examination otherwise normal.

A provisional *diagnosis* of lobar pneumonia, left, and empyema (?) was made. Suspicious signs of empyema were reported by röntgenogram taken the next day.

The patient's condition became progressively worse. Nine days after admission (September 28) a left thoracentesis was done and yielded about 5 cubic centimetres of thick pus. Culture of the pus returned a pneumococcus.

The operation of open drainage of the left pleural cavity was performed eight days after thoracentesis (October 6). Without anæsthesia an intercostal incision was made in the eighth left interspace and scissors were forced through the pleura into a large empyema cavity, from which much thick pus ran out. Two drains were placed in the cavity.

The post-operative condition was better for about a week, but was progressively worse thereafter. A röntgenogram taken October 14 showed no signs of fluid, however.

November 11 fluid was discovered in the right chest. Marked emaciation was also present. The next day, thirty-five days after the first operation, an *operation* was performed for open drainage of the right chest using the same technic as on the left. Pus was obtained; it was sterile.

Following operation there was no improvement, and the child died eight days after the second operation (November 20).

# BILATERAL PLEURAL EMPYEMA

## CASE REPORTS OF BILATERAL EMPYEMA, 1910 TO 1930

| 1<br>Author and<br>year  | 2 3<br>Patient |     | 4<br>Days from<br>diagnosis of<br>empyema<br>until first<br>operation | 5<br>Primary disease   | 6<br>Organism<br>cultured<br>from<br>empyema | 7<br>Type of drainage   | 8<br>Days<br>be-<br>tween<br>opera-<br>tions | 9<br>Re-<br>sult |
|--|----------------|-----|---|--|--|---|--|------------------|
|  | Age            | Sex |   |  |  |   |  |                  |
| 1.<br>Edmond<br>1910 <sup>23</sup>                             | 5              |     |   | Pertussis;<br>broncho-pneu-<br>monia   | ?  | 1—Right, open<br>2—Left, open   | 7  | C                |
| 2.<br>Corner and<br>Grant<br>1911 <sup>24</sup>                | 29             | F   | 0   | ?  | ?  | 1—Right, open; re-<br>section of rib<br>2—Left, open; re-<br>section of rib                             | 1  | C                |
| 3.<br>Gand and<br>Poissonier<br>1911 <sup>25</sup>             | 4              | M   |   | "Grippe"; pneu-<br>monia   | ?  | Open, simultaneous  | 0  | C                |
| 4.<br>Bozzotti<br>1913 <sup>2</sup>                            | 25             | F   | 11  | ?  | ?  | 1—Left, open; rib<br>resection<br>2—Right, open; rib<br>resection                                       | 5  | C                |
| 5.<br>Zingher<br>1913 <sup>26</sup>                            | 6.5            | M   | 0   | Bilateral<br>bronchopneu-<br>monia   | Pneumo-<br>coccus                            | 1—Left, open; re-<br>section 8th rib<br>2—Right, open; in-<br>tercostal incision<br>and drainage        | 26   | C                |
| 6.<br>Mackenzie<br>1914 <sup>3</sup> and<br>1924 <sup>27</sup> | 34             | M   |   | "Influenza"  | ?  | Open, simultaneous  | 0  | C                |
| 7.   | ?              | M   |   | "Influenza"  | ?  | 1—Right, open<br>2—Left, open   | 1  | C                |
| 8.   | ?              | M   |   | "Influenza"  | ?  | 1—Right, open<br>2—Left, open   | 1  | C                |
| 9.   | 7              |     | 0   | ?  | ?  | Open, simultaneous  | 0  | C                |
| 10.<br>Bunts<br>1914 <sup>28</sup>                             | 13             | ?   | ?   | Acute appendi-<br>citis, operation;<br>pleural pneu-<br>monia                        | ?  | 1— ? open<br>2— ? open  | ?  | C                |
| 11.<br>Lund and<br>Morrison<br>1916 <sup>29</sup>              | 16             | F   | 7   | Left lower lobar<br>pneumonia;<br>right middle<br>and lower lobar<br>pneumonia       | ?  | 1—Left, open; 9th<br>rib resected<br>2—Right, open  | 1  | C                |
| 12.<br>Cafritz<br>1918 <sup>16</sup>                           | ?              | F   | ?   | "Grippe"   | ?  | 1—Left, open; 8th<br>rib resection<br>2—Right, open   | 23   | C                |
| 13.<br>Norrlin<br>1919 <sup>30</sup>                           | 8              | F   | 11  | Pneumonia  | Diplococcus<br>pneumo-<br>coccus?            | 1—Right, open; 8th<br>intercostal inci-<br>sion<br>2—Left, open; same<br>technic                        | 28   | C                |
| 14.<br>Gundrum<br>1920 <sup>31</sup>                           | 26             | M   | 22  | Left lower lobar<br>pneumonia;<br>right lower<br>lobar                               | Pneumococ-<br>cus<br>type IV                 | 1—Right, closed;<br>#18 F. catheter in<br>10th right inter-<br>space<br>2—Left, closed;<br>same technic | 25   | C                |
| 15.<br>Durham<br>1920 <sup>32</sup>                            | 14             | M   | 8   | Influenza; otitis<br>media; bilat.<br>mastoiditis;<br>bilat. parotitis;<br>pneumonia | Staphylococ-<br>cus aureus                   | 1—Left, open; 9th<br>rib resected; re-<br>peated aspirations<br>2—Right, open; 8th<br>rib resected      | 42   | C                |

## E. LAWRENCE KEYES

CASE REPORTS (*Continued*)

| 1<br>Author and<br>year                         | 2 3<br>Patient |     | 4<br>Days from<br>diagnosis of<br>empyema<br>until first<br>operation | 5<br>Primary disease  | 6<br>Organism<br>cultured<br>from<br>empyema | 7<br>Type of drainage   | 8<br>Days<br>be-<br>tween<br>opera-<br>tions | 9<br>Re-<br>sult |
|---|----------------|-----|---|---|--|---|--|------------------|
|   | Age            | Sex |   |   |  |   |  |                  |
| 16.<br>Glenn<br>1920 <sup>33</sup>              | Child          | ?   | ?   | Left empyema fol-<br>lowed by right   | ?  | ?   | ?  | D                |
| 17.   | Child          | ?   | ?   | Left empyema fol-<br>lowed by right   | ?  | ?   | ?  | D                |
| 18.<br>Jehn<br>1921 <sup>34</sup>               | 24             | F   | 14  | Pneumonia, left   | ?  | 1—Left, closed; rib<br>resection<br>2—Right, closed; rib<br>resection                                       | 11   | D *              |
| 19.   | 50             | F   | ?   | Bilateral encap-<br>sulated empy-<br>ema                                    | ?  | Both sides drained;<br>methods not<br>stated  | ?  | C                |
| 20.<br>Ladd and<br>Cutler<br>1921 <sup>35</sup> | Child          | ?   | ?   | ?   | ?  | Simultaneous bilat-<br>eral open drainage   | 0  | C                |
| 21.   | Child          | ?   | ?   | ?   | ?  | Simultaneous bilat-<br>eral open drainage   | 0  | C                |
| 22.   | Child          | ?   | ?   | ?   | ?  | ?   | ?  | D                |
| 23.<br>Stenius<br>1920 <sup>36</sup>            | ?              | ?   | ?   | ?   | ?  | ?   | 25   | C                |
| 24.<br>Schweizer<br>1921 <sup>37</sup>          | 51             | ?   | ?   | A chronic empy-<br>ema, probably<br>of tuberculous<br>origin                | ?  | ?   | ?  | D                |
| 25.<br>Beck<br>1921 <sup>17</sup>               | 36             | F   | ?   | Influenza; bilat-<br>eral broncho-<br>pneumonia;<br>pregnancy, 8th<br>month | ?  | 1—Right, closed in-<br>tercostal, followed<br>21 days later by<br>resection of 8th<br>rib<br>2—Left, closed | 24   | C                |
| 26.<br>Andrenelli<br>1923 <sup>38</sup>         | 43             | M   | ?   | Abdominal symp-<br>toms; retention<br>of urine                              | ?<br>Exudate was<br>serofibrinous            | No operation; re-<br>peated aspirations   | ?  | C                |
| 27.<br>Auer<br>1925 <sup>39</sup>               | 8              | F   | 2 (?)   | Acute respiratory<br>infection;<br>pneumonia                                | Pneumococ-<br>cus                            | 1—Right, open (?)<br>with rib resection;<br>repeated aspira-<br>tions<br>2—Left, closed                     | 16   | C                |
| 28.<br>Hedblom<br>1925 <sup>40</sup>            | 19<br>mos.     | M   | ?   | Bronchopneu-<br>monia   | ?  | 1—Right, closed (?)<br>with rib resection<br>2—Left, closed (?)<br>with intercostal<br>drainage             | ?  | C                |
| 29.<br>Mackey<br>1925 <sup>41</sup>             | 29             | M   | 1 (?)   | Lobar pneumo-<br>nia rt. lung and<br>left lower lobe                        | Pneumococ-<br>cus and pneu-<br>mobaillus     | 1—Left, closed;<br>costal drainage<br>2—Right, closed; in-<br>tercostal drainage                            | 22   | C                |
| 30.<br>Matthews<br>1927 <sup>42</sup>           | 5              | M   | ?   | Pneumonia, left<br>(lobar)  | Streptococ-<br>cus viridans                  | 1—Left, closed (in-<br>tercostal drainage)<br>2—Right, closed<br>(intercostal drain-<br>age)                | 17   | C                |

# BILATERAL PLEURAL EMPYEMA

## CASE REPORTS (Continued)

| 1<br>Author and<br>year                             | 3<br>Patient |     | 4<br>Days from<br>diagnosis of<br>empyema<br>until first<br>operation | 5<br>Primary disease  | 6<br>Organism<br>cultured<br>from<br>empyema  | 7<br>Type of drainage   | 8<br>Days<br>be-<br>tween<br>opera-<br>tions | 9<br>Re-<br>sult |
|---|--------------|-----|---|---|---|---|--|------------------|
|   | 2<br>Age     | Sex |   |   |   |   |  |                  |
| 31.<br>Graves<br>1928 <sup>43</sup>                 | 6            | F   | 4   | Acute appendicitis; appendectomy; (tertian malaria); lobar pneumonia, right upper | Pneumococcus  | 1—Right, open, with rib resection<br>2—Left, open, with rib resection           | 5  | C                |
| 32.<br>Scanlan<br>1928 <sup>1</sup>                 | 21           | F   | 11  | Lobar pneumonia, both lower lobes   | B. Coli   | 1—Left, closed (intercostal drainage)<br>2—Right, closed (intercostal drainage) | 3  | C                |
| 33.<br>Tixier and<br>de Sèze<br>1929 <sup>44</sup>  | 8            | M   | 2   | Lobar pneumonia, left<br>Lobar pneumonia, right                                   | Pneumococcus  | 1—Left, open, with rib resection<br>2—Right, closed                             | 63   | C                |
| 34.<br>Ravnitzky<br>and Bogin<br>1930 <sup>45</sup> | 5            | F   | ?   | Pneumonia   | ?   | 1—Right, intercostal<br>2—Left, rib resection                                   | 33   | C                |
| 35.   | 17 mo.       | F   | ?   | Pneumonia, both sides   | ?   | No operation; repeated aspirations; brain abscess                               |  | D                |
| 36.   | 2½           | M   | 5   | Otitis media; acute lobar pneumonia, both bases and right middle                  | Pneumococcus  | 1—Left, intercostal drainage<br>2—Right, rib resection                          | 37   | C                |
| 37.   | 8            | F   |   | Bronchopneumonia  | Pneumococcus  | 1—Right, rib resection<br>2—Left, rib resection                                 | 26   | C                |
| 38.   | 1            | F   |   | Pneumonia (lobar) left upper and right base                                       | Streptococcus   | Left, chest tapped; no operation  |  | D                |
| 39.<br>Keyes<br>Case 2<br>above                     | 17           | M   | ?   | Bronchopneumonia  | Pneumococcus, type II (Right side also showed streptococcus viridans and staphylococcus aureus) | 1—Right, open, with rib resection<br>2—Left, open, with rib resection           | 45   | C                |
| 40.<br>Case 3<br>above                              | 2¾           | M   | ?   | Lobar pneumonia, left   | Pneumococcus  | 1—Left, open; intercostal drainage<br>2—Right, open; intercostal drainage       | 37   | D                |
| 41.<br>Case 4<br>above                              | 2            | F   | 6   | Bronchopneumonia  | Pneumococcus, type I  | 1—Right, closed; intercostal drainage<br>2—Left, closed; intercostal drainage   | 12   | C                |

\* Death from intercurrent infection. Autopsy showed caseous tuberculosis of left side.



SUMMARY AND CONCLUSIONS

1. Forty-one cases of bilateral empyema occurring from 1910 to 1930, three previously unreported, are summarized.
2. The natural history and treatment of the disease are outlined.
3. The literature since the last complete reports is reviewed.
4. Attention is called to simultaneous bilateral thoracotomies as an advisable method of treatment under certain circumstances.
5. It is recommended that the second side be drained very soon after the first.
6. The initial drainage should be of the closed type.

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## SUBCUTANEOUS RUPTURE OF THE SPLEEN\*

TWO CASES WITH BLOOD COUNTS FOLLOWING SPLENECTOMY†

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FROM THE SURGICAL SERVICES OF THE KNICKERBOCKER AND ST. LUKE'S HOSPITALS

THESE cases are reported particularly because of their normal blood counts following splenectomy. Without going into individual case reports, the impressions obtained by reading the literature listed at the end of this article might be briefly stated as follows (considering only those cases from which a ruptured normal spleen had been removed):

In the early days of splenectomy when clamps were left on the pedicle, large packs were placed down to the pedicle, or large drains were inserted as routine procedure, a persistently high total and polymorphonuclear count was invariably noted. If the time when the wound became clean was noted, this time checked with the time at which the leucocyte count became normal. A severe secondary type of anæmia was always reported which required months to return to normal. This is readily explained by the original hæmorrhage followed by the depletion from the large infected draining wound.

In more recent literature the severity of these two conditions is given less emphasis. Instead there is reported usually an immediate polymorphonuclear leucocytosis, often a lymphocytosis, and in many cases a transient anæmia of the secondary type. Several men report an increasing eosinophilia following removal of the spleen. Others report a moderate anæmia lasting for years.

CASE I.—J. McM., aged fifteen years, was admitted to Knickerbocker Hospital, February 1, 1928. One hour before admission, while coasting down a hill, he had struck an electric light pole. Immediately, he noticed a severe pain in the upper abdomen associated with nausea and vomiting. This was followed within a few minutes by a feeling of faintness.

Examination was that of a white boy in extreme shock. His pulse was 140, temperature 97°, and respirations 30. No external evidence of injury could be found except a small contusion on the left lateral chest wall two inches above the costal margin. The chest findings were otherwise normal but for rapid shallow respirations with less excursion of the diaphragm on the left than on the right. The abdomen was generally rigid, with the rigidity most marked in the upper left quadrant. The right flank was tympanitic; the left was dull. This dullness extended upward to a greatly increased area of splenic dullness.

The urine was normal but for an occasional red blood cell. The admission blood count was: Red blood cells 3,770,000 hæmoglobin 65, white blood cells 23,400, polymorphonuclear leucocytes 84, and lymphocytes 16.

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\* Presented before the Surgical Section of the New York Academy of Medicine, May 2, 1930.

† Blood counts to December 6, 1930.

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Operation was done immediately with a pre-operative diagnosis of ruptured spleen.

Under ether anæsthesia, the abdomen was opened through an upper left rectus incision. Fresh fluid blood showed as soon as the peritonæum was incised. One-half of the spleen was found in the lower right quadrant near the cæcum, still attached to the pedicle by a long narrow strip of peritonæum. This attachment did not contain any blood-vessels large enough to be seen. The other half of the spleen was in its normal location.

There was a tear about three inches long in the lesser omentum and another in the peritonæum of the lateral abdominal wall, beneath which was a small hæmatoma. The kidney was not examined. No damage to the tail of the pancreas was apparent. Two small accessory spleens were noted attached to the pedicle of the spleen and were left undisturbed. They were each about the size and shape of a navy bean.

The pedicle was long enough to be clamped and cut. It was then transfixed and ligated twice. The pedicle and the two tears in the peritonæum were peritonized. The abdomen was closed in layers without drainage. Immediately following the operation 800 cubic centimetres of whole blood were transfused by the Soresi method.

Convalescence was uneventful except that, on the fourth day, by some mistake, the skin and tension sutures were all removed by one of the internes. The wound opened up to the fascia. It was closed with strips of adhesive and healing occurred without further complication. A very firm scar resulted.

This patient has been followed at regular intervals since. His health and growth have been normal. Aside from an occasional slight cold he has had no illnesses. The blood counts are shown on the accompanying chart.

### CASE I

|                     | Hgb. | Red b.c.   | Leucocytes | Polys. | Lymph. | Misc. |
|---------------------|------|--|------------|--------|--------|-------|
| Pre-op.             |      |  |            |        |        |       |
| Half-hour . . . . . | 65   | 3,770,000  | 23,400     | 84     | 16     |       |
|                     |      | (800 cc. whole blood Soresi method immediately post-op.) |            |        |        |       |
| Post-op.            |      |  |            |        |        |       |
| 1st day . . . . .   | 88   | 4,400,000  | 11,200     | 80     | 20     |       |
| 18th day . . . . .  | 88   | 4,400,000  | 12,800     | 78     | 22     |       |
| 6 mos. . . . .      | 95   | 4,800,000  | 9,200      | 75     | 25     |       |
| 15 mos. . . . .     | 100  | 5,100,000  | 8,600      | 70     | 30     |       |
| 24 mos. . . . .     | 100  | 6,400,000  | 10,600     | 72     | 28     |       |
| 27 mos. . . . .     | 106  | 5,590,000  | 9,700      | 56     | 41     | E. 3  |
| 32 mos. . . . .     | 100  | 5,700,000  | 9,600      | 60     | 39     | E. 1  |
| 34 mos. . . . .     | 104  | 5,500,000  | 7,800      | 54     | 44     | E. 2  |

CASE II.—M. L., aged eight years, was admitted to St. Luke's Hospital at 5:15 p.m., December 7, 1929. Two hours before admission, while he was trying to help move a large touring car, the car suddenly backed and the rear wheel passed over his abdomen. He was brought into the hospital because of the increasing pain in the upper abdomen. Immediately after admission about a pint of fairly fresh blood was vomited.

Examination was that of an acutely ill white boy, suffering severe pain in the upper abdomen. He was quite pale. His pulse was 116, temperature 98.4°, and respirations 20. The only external evidence of injury was a bruised area over the right anterior superior iliac spine about which was an ecchymosis, measuring approximately 1 by 2 inches.

The chest was normal but for limited excursion of the diaphragm. The abdomen was generally tender to pressure, with rigidity of both recti above the umbilicus. This was most marked on the right side. No masses could be palpated. Both flanks were tympanitic. There was a questionable increase in the liver dulness in the mid-line.

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As the patient did not think that he had voided since the accident and was unable to do so, he was catheterized. Two ounces of normal urine were obtained. The admission blood count was: Red blood cells 3,850,000, hæmoglobin 76, white blood cells 24,300, polymorphonuclear leucocytes 84, and lymphocytes 16.

At 6:10 P.M. patient again vomited a considerable quantity of fairly fresh blood.

At 6:35 P.M. he was much worse. His physical findings were unchanged except that the tenderness and rigidity in the right upper abdomen had increased. Operation was then done immediately. The pre-operative diagnosis was retroperitoneal rupture of the duodenum because of the location of the increasing tenderness and rigidity, and the vomiting of blood without any obliteration of the liver dulness. The absence of dulness in the left flank apparently excluded rupture of the spleen unless it had occurred with very little hæmorrhage.

Field block and local infiltration with novocain was used. The abdomen was opened through the upper right rectus muscle. There was fresh blood beneath the peritonæum, but no gas. The liver surfaces were smooth. Anteriorly the stomach and transverse colon were normal. No blood came from the lesser omental sac. A large amount of fresh blood and clots were found high up under the left costal arch and in this the spleen was felt divided into two separate portions. The tail of the pancreas was not visibly injured.

The incision was extended upward. Traction on the abdominal wall made the patient very uncomfortable, so that he was given ether for the remainder of the operation. By retracting the left side of the incision, the pedicle of the spleen could be exposed quite readily. It was transfixed and ligated doubly. The spleen was then cut away and the stump peritonized. A small rent in the lesser omentum was closed and the edges covered with peritonæum.

No further exploration was done. The abdomen was closed in layers without drainage. An infusion of 500 cubic centimetres of normal saline was given during the operation. A transfusion of 750 cubic centimetres of whole blood was given by the Lindeman method before the patient left the operating table.

Because of the possibility of an undiscovered retroperitoneal injury to the stomach or duodenum, nothing was given by mouth for the first four days. During this time

## CASE II

|                    | Hgb. | Red b.c.   | Leucocytes | Polys. | Lymph. | Platelets | Misc.  |
|--------------------|------|--|------------|--------|--------|-----------|--------|
| Pre-op.            |      |  |            |        |        |           |        |
| 1 hour . . . . .   | 76   | 3,850,000  | 24,300     | 84     | 16     |           |        |
|                    |      | (750 cc. whole blood Lindeman method immediately post-op.) |            |        |        |           |        |
| Post-op.           |      |  |            |        |        |           |        |
| 1st day . . . . .  | 83   | 4,500,000  | 13,300     | 78     | 22     |           |        |
| 2nd day . . . . .  | 93   | 4,600,000  | 10,500     | 86     | 14     |           |        |
| 3rd day . . . . .  | 86   | 4,500,000  | 9,000      | 82     | 18     |           |        |
| 4th day . . . . .  | 93   | 4,550,000  | 9,900      | 82     | 17     |           | E. 1   |
| 5th day . . . . .  | 88   | 4,250,000  | 15,000     | 82     | 20     |           |        |
| 6th day . . . . .  | 88   | 4,300,000  | 14,000     | 78     | 22     |           |        |
| 8th day . . . . .  | 84   | 4,300,000  | 9,200      | 75     | 25     |           |        |
| 19th day . . . . . | 98   | 4,900,000  | 7,200      | 43     | 55     | 350,000   | E. 2 * |
| 1½ mos. . . . .    | 90   | 4,950,000  | 6,950      | 50     | 47     |           | E. 3   |
| 3½ mos. . . . .    | 88   | 4,800,000  | 8,000      | 64     | 36     | 270,000   |        |
| 4½ mos. . . . .    | 83   | 4,500,000  | 8,000      | 72     | 26     | 165,000   | Mon. 2 |
| 10 mos. . . . .    | 83   | 3,750,000  | 5,200      | 54     | 44     | 180,000   | E. 2   |
| 12 mos. . . . .    | 70   | 4,500,000  | 11,000     | 65     | 34     | 230,000   | E. 1   |

\* Reticulated red blood cells 2 per cent. Few young polymorphonuclear leucocytes.

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normal salt and 5 per cent. glucose solutions were given by hypodermoclysis every eight hours. He was then put on the regular gastric post-operative routine. (Gastro-intestinal röntgenograms made three months later showed no pathology.)

Convalescence was uneventful. His health and growth have been normal since the operation. He has had no illnesses. His indoor life in the city probably accounts for the moderate secondary anæmia in the last two counts.

### SUMMARY

Two cases of subcutaneous rupture of the spleen are reported which were treated by splenectomy without drainage. In both, the large whole blood transfusion evidently replaced the blood lost by hæmorrhages. These resulting red counts were maintained. The leucocyte count and differential do not appear to be other than would be expected following any similarly large operation. However, in both cases eosinophiles do appear in the later counts but not to an abnormal percentage.

The possibility of a difference between the two cases is suggested by the last counts. Case I has maintained this high count. He had two small accessory spleens. In Case II the last two counts show a moderate secondary anæmia. No accessory spleens were noted in this case. Additional counts in the future on these two patients may prove very interesting for this reason.

DISCUSSION.—DR. ELSWORTH ELIOT, JR., remarked that in 1907 two cases of splenectomy for subcutaneous rupture of the spleen were reported by him to the American Surgical Association. At that time the number of cases in surgical literature were few in number and, in the still fewer instances of recovery, were without mention of any ultimate change in the composition of the blood as well as in the general condition of the patient. In the paper referred to, examination of the blood of both patients a year after operation showed little change from the normal. Whether or not the loss of the spleen was followed by any constitutional disturbance, including diminished resistance to infections, was also discussed, showing that usually any impairment was transitory and that eventually patients returned to a normal condition. This is to be accounted for by the gradual compensatory increase in adenoid or lymphoid tissue and in the bone marrow, as well as in the enlargement of small frequently unobserved accessory spleens occasionally present in the gastro-hepatic omentum. Such accessory spleens, no larger than a small finger-tip, were later observed in a boy of ten in whom a splenectomy was performed for rupture, in whom examination of the blood one year later proved quite normal. That this favorable outcome does not always obtain was recently observed in the case of a previously strong young man who, one year after splenectomy for rupture, showed a marked tachycardia with a hæmic murmur. As an electrocardiogram proved normal, the ultimate prognosis in this instance is probably favorable.

He called attention to the second case reported by Doctor Shelley because of the more pronounced evidence of peritoneal irritation on the right side. Ordinarily the tenderness in the left flank, increased by pressure on unbroken eleventh and twelfth ribs, the dulness or flatness, especially on auscultation in the left ilio-costal space and the rigidity of the left rectus, especially in its upper portion, have proved the most reliable physical signs. Of unusual occurrence is to be mentioned the upward displacement of the apex beat of the heart. This was noted in one case seen by him in which the accumulated blood in the peritoneal cavity was relatively small in amount.

As to treatment, all agree that splenectomy at the earliest possible moment is the operation of choice. That in certain cases the spleen may be conserved is quite true. Thus in a young girl of twelve who had merely slipped off her pony on to soft turf, the symptoms were so slow and insidious that the abdomen was not explored until the third day after the accident. At that time bleeding had ceased and, after the clotted blood was removed, a tampon of gauze was introduced to forestall the possibility of a renewal of the hæmorrhage, with a successful result. In cases, however, where indications of alarming hæmorrhage develop rapidly, splenectomy must be regarded as the only procedure.

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## INTRA-ABDOMINAL APOPLEXY

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FROM THE SURGICAL CLINIC OF THE PETER BENT BRIGHAM HOSPITAL

SPONTANEOUS rupture of arteriosclerotic vessels within the abdomen is extremely rare. A patient recently operated on by us presented this unusual and striking pathological picture, *i.e.*, rupture of a major branch of the left gastric artery with a dissecting hæmatoma of the gastro-hepatic omentum and a large amount of blood in the peritoneal cavity. A search through the literature has disclosed only two similar cases of hæmoperitonæum actually demonstrated at the operating table, one case which was comparable save for the fact that the ruptured vessel was not located, and one case in which operation was not performed.

Gross aneurisms of visceral arteries are found with comparative frequency and occasionally rupture. Spontaneous rupture of vessels of the extremities<sup>2</sup> has been reported and Lincoln<sup>6</sup> has recorded rupture of the renal artery retroperitoneally. Traumatic rupture of abdominal vessels likewise occurs not infrequently.<sup>7</sup> None of these conditions, however, may be classified as true intra-abdominal apoplexy.

### REPORT OF CASES

CASE I.—*Authors'*—M. M. K., Surg. No. 35362. A widow, fifty-four years of age, entered the hospital complaining of severe abdominal pain of five hours' duration.

*Past History.*—The patient sustained an intra-ocular hæmorrhage five years previously. Three years later she sought medical advice because of loss of weight and epistaxis. During the past year she had had occasional attacks of sudden, sharp pain in the precordium, radiating to the left shoulder and gradually increasing in frequency. Six months prior to admission she was told by her local doctor that her systolic blood-pressure was 270. Rest was advised but was not carried out. A gradual loss of forty pounds in weight had occurred during the past two years. There was no history of epigastric distress; there were no bloody, tarry, or clay-colored stools. Her appetite was good and her bowels were regular with saline catharsis.

*Present Illness.*—While preparing her supper, five hours previous to admission, the patient was seized with a sudden attack of very sharp pain in the mid-epigastrium, rapidly spreading over the entire abdomen. The pain was prostrating in character, constant and agonizing. Nausea developed and she vomited a small amount of clear fluid.

*Physical Examination.*—A well-developed but poorly nourished, elderly white woman lying in bed with her knees drawn up, obviously in pain. The skin was dry, somewhat wrinkled, but not unduly warm. The heart was enlarged to the left and a rough systolic murmur was audible at the apex. The aortic and pulmonic sounds were of about equal intensity. The peripheral vessels were sclerotic. The systolic blood-pressure was 170, the diastolic was 110. Palpation of the abdomen revealed a board-like rigidity throughout with diffuse tenderness of marked degree, most intense in the epigastrium. No fluid could be demonstrated in the peritoneal cavity. Hepatic dulness was normal. Vaginal and rectal examination disclosed tenderness in both lateral pelvic vaults.

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*Clinical Pathology.*—On admission the temperature was 99.4 degrees by rectum, the pulse rate was 100, and the respiratory rate, 20. The leucocyte count was 16,000 and 20,000 at two examinations. The urine showed a large trace of albumen and a slight trace of sugar. The sediment contained numerous hyaline casts, occasional leucocytes and red blood cells.

Pre-operative diagnosis was cardiorenal-vascular disease and either perforated peptic ulcer, acute pancreatitis, or perforated carcinoma of the stomach.

*Operation.*—Ligation of branch of left gastric artery, partial evacuation of hæmatoma of gastro-hepatic omentum, removal of blood from the peritoneal cavity; novocain and ether anæsthesia.

After a preliminary dose of morphia and scopolamin, the abdominal wall was infiltrated with novocain and opened through an upper right rectus incision. Bloody fluid escaped immediately after incising the peritoneum. Light anæsthesia with ether was then

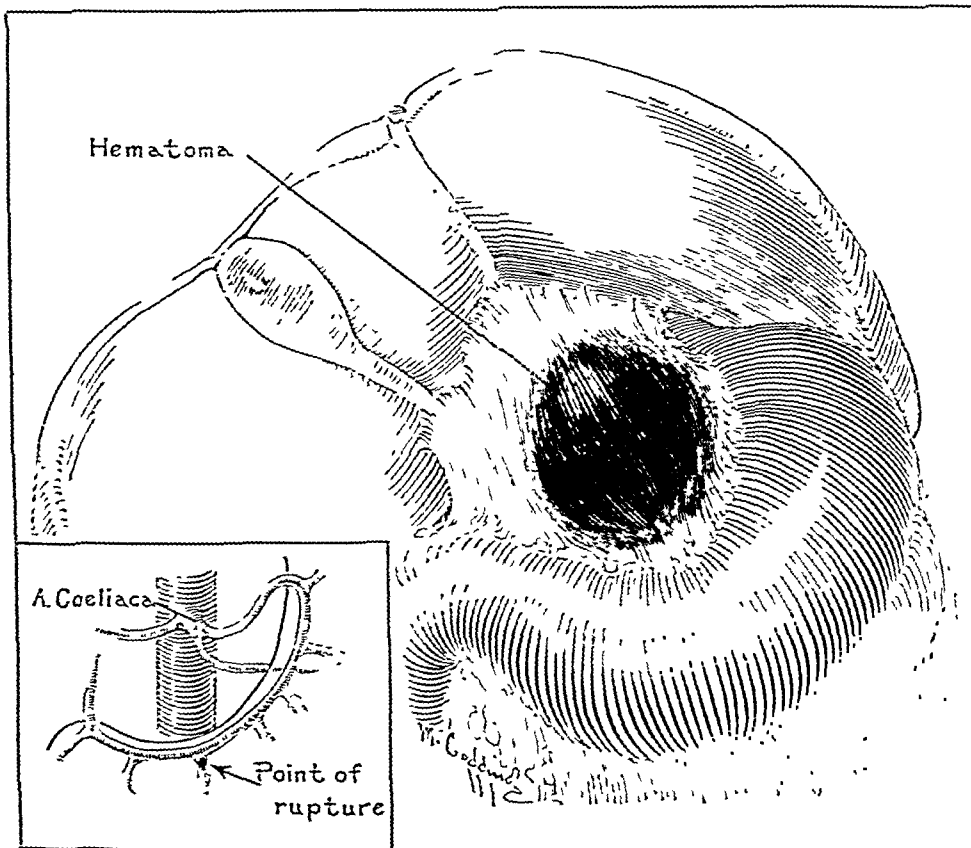


FIG. 1.—Hæmatoma of the gastro-hepatic omentum. Insert shows the point of rupture in a primary branch of the left gastric artery.

induced and a careful exploration was carried out. A large hæmatoma was found in the gastro-hepatic omentum, extending from the mid-portion of the lesser curvature of the stomach upward to the cardia and outward for approximately 3 inches (Fig. 1). The anterior leaf of the omentum was incised near the lesser curvature, the hæmatoma was partially evacuated, and a sclerotic branch of the left gastric artery was found to be ruptured and bleeding smartly. Ligatures were placed around the vessel on each side of the bleeding point and the hæmorrhage ceased. The abdomen was closed with drainage. At the end of the operation the systolic blood-pressure was 180, the diastolic, 100. The patient's general condition was good.

*Post-operative Course.*—Five hours later the systolic blood-pressure was 260, the diastolic, 135. There was no post-operative vomiting and no abdominal distension. Drainage from the wound was slight. An intravenous phthalein test on the sixth day showed a renal function of 40 per cent. The convalescence was unremarkable. The patient's

general condition improved, the blood-pressure gradually subsided, and she was discharged on the thirty-third post-operative day. The wound was firmly healed; the temperature, pulse rate and respiratory rate were normal; the leucocyte count was 9,300; the systolic blood-pressure was 160 and the diastolic, 95.

*Subsequent Note.*—The patient was seen eight months later. During this interval she had been well except for occasional headaches. Her blood-pressure was, systolic, 260, diastolic, 145. Abdominal examination was entirely negative. The wound was well healed.

CASE II.—*Starcke*.<sup>8</sup>—A man, sixty years of age, entered the hospital because of severe epigastric pain. The past history included gastro-intestinal symptoms for many years, characterized by eructations of gas, nausea, constipation and occasional diarrhoea. Dyspnoea and palpitation had been prominent during the two years prior to admission.

Physical examination disclosed an elderly man in severe pain. The skin was cold and clammy. The heart was enlarged; a systolic murmur, maximal at the apex, and many extra systoles were audible. The radial arteries were palpably sclerotic. The abdomen was rigid and tenderness was marked, particularly in the epigastrium. Deep palpation was impossible. There was no discernible dullness in the flanks. The temperature was 99.4 degrees.

Operation was performed immediately. The omental bursa was filled with blood which was escaping into the general peritoneal cavity through the foramen of Winslow. A rupture of the gastro-duodenal artery was found to be the cause of the hæmorrhage. The bleeding point was grasped and ligated.

The post-operative course was uncomplicated and two months later the patient was in relatively good health. The systolic blood-pressure was 155.

CASE III.—*Budde*.<sup>3</sup>—A man, twenty-seven years of age, previously well, suddenly developed severe pain in the left hypochondrium. When admitted to the hospital several hours later tenderness and spasm of the abdominal wall were generalized but most marked in the left upper quadrant. A tentative diagnosis of perforation of the stomach or acute pancreatitis was made.

Abdominal exploration revealed liquid blood throughout the peritoneal cavity and large clots in the left hypochondrium. Further investigation disclosed a rupture in one of the branches of the left gastro-epiploic artery. A huge hæmatoma of the omentum was found in this region. The bleeding point was ligated and recovery was complete. The patient was in good health six months later.

CASE IV.—*Hilliard*.<sup>6</sup>—A man, aged forty-eight years, was seized with severe epigastric pain one hour before admission to the hospital. During the previous eight years he had had attacks of dizziness, and headaches associated with marked arteriosclerosis and some loss of power in the lower extremities. During this period, the systolic blood-pressure had varied between 160 and 190. Three years prior to admission he sustained a left hemiplegia from which he had largely recovered.

When admitted the patient was in very severe pain. The abdomen was distended, rigid, and board-like. There was dullness in both flanks; percussion of the liver was normal. The pulse rate was 80; the temperature was subnormal.

Abdominal exploration was performed. The peritoneal cavity was filled with blood. "Hæmorrhagic patches were scattered over the mesocolon." There was no evidence of fat necrosis. No bleeding vessel was found and the abdomen was closed. The patient died six hours later.

CASE V.—*Ducuing and Florence*.<sup>4</sup>—A young woman, eight months' pregnant and seriously ill, was admitted to the hospital because of generalized abdominal pain associated with complete obstipation of forty-eight hours' duration. The respiratory rate was 50, the pulse rate, 90. Considerable flatus and a small amount of fæcal material were obtained after the administration of an enema. The patient was in labor at entry and parturition was completed four hours later.

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Her condition did not improve. The abdominal wall was spastic and signs of free fluid were noted. A puncture was made in the pouch of Douglas and blood was obtained. Operation was not performed. The patient died.

Post-mortem examination disclosed blood throughout the general peritoneal cavity. A rupture was found in one of the branches of the superior mesenteric artery with early gangrene of the bowel along the distribution of this vessel.

No statement was made concerning the condition of the vascular system.

*Comment.*—The case reported by Starcke was entirely comparable to our own except for the site of hæmorrhage. The case of Budde was likewise similar although the author did not record the patient's blood-pressure nor comment on the presence of evident arterial disease. Hilliard's case was comparable in symptoms and operative findings although the actual bleeding vessel was not found. Post-mortem examination was not made and consequently definite proof that the case should be included in this group is absent. The case of Ducuing and Florence was not reported in detail. The accident occurred during labor and the ruptured vessel was found only at autopsy. No comment was made concerning the condition of the vascular system. Whether or not the case should be included in this series or classified as a traumatic complication of labor is uncertain.

It seems unusual that intra-abdominal apoplexy does not occur more frequently. Allbutt<sup>1</sup> has pointed out that the cerebral and visceral arteries are similarly affected in the type of arteriosclerosis which occurs in "essential hypertension." In these cases, next to cardiac complications, cerebral apoplexy is the most common cause of death, yet an abdominal lesion of this type is almost unknown. The relatively frequent incidence of cerebral lesions may depend in part on the variance in anatomical structure of the vessels in the two areas, and in part on the fact that a minute hæmorrhage in the cranial cavity is productive of symptoms out of all proportion to the actual lesion. A similar process within the abdominal cavity may remain entirely unrecognized.

In reviewing these cases certain salient features may be emphasized.

1. Three of the patients presented both historical and clinical evidence of vascular disease. They were hypertensive and showed a marked degree of arteriosclerosis. In the remaining two cases the authors made no comment concerning the condition of the vascular system.

2. The outstanding symptom in each case was sudden and severe abdominal pain, prostrating in character and most intense above the level of the umbilicus. The mechanism of this symptom must depend partly on the irritation of the peritonæum by blood and, in two cases at least, on the distension of the omentum by a dissecting hæmatoma.

3. Physical findings were uniformly marked by a state of partial shock and by the presence of an extremely tender and rigid abdomen.

4. A presumptive diagnosis of perforated peptic ulcer, or acute pancreatitis was made in all cases and, in retrospect, there seems to be no method of differentiation. The evidence of marked vascular disease and the absence

of previous gastro-intestinal symptoms offer the only clue to the true nature of the disease.

*Summary.*—A case of spontaneous rupture of a primary branch of the left gastric artery has been recorded. Only four comparable cases have been found in the literature. These patients presented symptoms and physical findings which suggested a pre-operative diagnosis of perforated peptic ulcer or acute pancreatitis. Abdominal exploration in four cases revealed a large hæmoperitonæum. The fifth was demonstrated at autopsy. In three instances the bleeding vessel was identified and ligated and the patients recovered. These cases have been classified under the general term of intra-abdominal apoplexy.

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## SUBPHRENIC ABSCESS\*

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SUBPHRENIC abscess, while not rare, is one of the less frequently encountered complications of peritonitis although, as is well known, it may arise secondarily to causes other than infection within the peritoneal cavity.

At the Pennsylvania Hospital from 1910 to 1926, ten cases were recorded and in an additional one, although the clinical and X-ray findings suggested that an abscess was present, in view of the fact that exploration was not done, the case is not included in the present series. No case of subphrenic abscess has been seen in this institution since 1926. At the Presbyterian Hospital, from 1922 to 1931 there were eight cases—a total of eighteen, and for the privilege of reporting these two groups I am indebted to the surgeons upon whose services they were admitted.

We fully realize that this is a very small series and that in presenting it we have nothing new to add, but thought that from the clinical aspect some of the cases might present features of interest and serve to promote a discussion among the members of this society.

As is well known, the majority of cases of subphrenic abscess arise secondary to a perforation of an abdominal viscus—stomach, duodenum, appendix or gall-bladder—but one must bear in mind that it may also result from an abscess of the spleen, liver, kidney, pancreas or spine; from traumatism, pyæmia and distant foci of infection, such as carbuncle, etc. In the group we are recording only seven cases actually followed a perforation of an abdominal viscus. It may also follow infection above the diaphragm; such as pneumonia, empyema, lung abscess, osteomyelitis of ribs, etc. In those cases in which the subphrenic abscess apparently follows an empyema thoracis, one must bear in mind the possibility of its having been caused by perforation of the diaphragm by the exploring needle, and of subsequent infection of the subphrenic region. When the stomach—exclusive of the pyloric region—the pancreas or the spleen is the primary focus, the subphrenic abscess is usually on the left side, most of the other sources giving rise to an abscess on the right.

It is not our intention to describe again in detail the anatomy of the subphrenic areas as nearly all of the recorded series of this type of abscess are accompanied by such a description with references to the excellent article by Barnard.<sup>1</sup> Those interested in this aspect of the subject are referred to the above paper and to one by Lockwood<sup>2</sup> of The Mayo Clinic. Sufficient to state that for practical purposes the subphrenic area may be

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\* Read before the Philadelphia Academy of Surgery, January 5, 1931.

divided into right and left anterior and posterior intraperitoneal; and right and left extraperitoneal spaces.

The diagnosis of subphrenic abscess often presents many features of interest, not the least difficult of which is the determination of whether the collection of pus lies above or below the diaphragm, or both; or whether the condition present is an abscess within the liver. In our experience the associated findings in the chest, such as secondary compression of the lung and changes in the breath sounds, tactile and vocal fremitus, "splashing" sounds on moving the patient, etc., are often quite confusing and may at times be misleading.

From the viewpoint of surgical diagnosis our chief reliance is based on the history of a preceding infection; more or less localized tenderness with possible fullness and induration over the involved area; evidence of pus somewhere in the body as shown by temperature range, leucocytosis, toxic condition of the patient, etc.; X-ray examination, and exploratory puncture. As has been emphasized by numerous writers, one of the chief reasons for not recognizing the condition is failure to consider the possibility of its existence.

Occasionally one encounters a case of subphrenic abscess in which there is no antecedent history of demonstrable infection, as was seen in the case of a man of twenty-seven years who entered the hospital complaining of swelling in his right chest wall. Five weeks before admission he noticed a small, painless, slightly reddened swelling over the anterior part of his right chest. His previous medical history was irrelevant and physical examination was essentially negative aside from the above-mentioned swelling which was about 15 by 20 centimetres in diameter, extending over the seventh, eighth and ninth ribs on the antero-lateral aspect of his chest. A subphrenic abscess was not suspected and unfortunately an X-ray of his chest was not taken. The pre-operative diagnosis was suppurative perichondritis.

Under local anæsthesia the abscess was incised with the escape of "an abundant amount of pus," which gave a positive culture for *B. coli communis*. Digital exploration revealed that the abscess had perforated through the eighth interspace and resection of the eighth rib uncovered an extensive subphrenic abscess cavity. Drainage was instituted and recovery was uneventful, he being discharged from the hospital on the twenty-fifth post-operative day.

In this instance it might be suggested that involvement of the rib was the primary focus but there was no history of previous injury, unrecognized typhoid or any other infection which would imply that the process started from the rib.

The question of sex is, we believe, incidental, thirteen males and five females, and aside from the fact that the condition is less apt to occur in children—four in the series being under ten years of age—age is apparently not of much importance. Its greater frequency in men is probably because perforation of an abdominal viscus is more frequently encountered in men than in women, and more so in adults than in children.

As was to be expected, most of the cases followed a previous operation. Thus five had had appendectomies which required drainage; two resulted

from perforation of a peptic ulcer. (During the period covered by this report there were one hundred and thirteen cases of perforated peptic ulcer operated upon in the Pennsylvania and Presbyterian Hospitals.) Two followed cholecystostomies; one arose subsequent to a cæcostomy; one as a sequence to puerperal fever with secondary abscess of the spleen; one followed an abdominal exploration in which no pathological condition could be demonstrated, the subphrenic abscess apparently being overlooked at the time, and in six instances there had not been any previous operation.

From the above figures it will be seen that eight of the eighteen cases occurred without evidence of demonstrable previous peritoneal infection. As an example of this latter group may be cited the case of H. B., an infant of twenty-two months, who was admitted to the hospital suffering with a "cold" following measles. The condition began as a "cold" of two weeks' duration, six weeks before admission. Measles, lasting two weeks, developed, and at the end of this period evidence of pneumonia was present. On examination of the chest dulness was detected at the right base both anteriorly and posteriorly; the heart was not displaced and the abdomen was somewhat distended. The temperature, pulse and respiration were 102°, 144 and 40 respectively. An X-ray of the chest made on the day of admission showed that the right and left sides of the diaphragm presented nothing abnormal, and the size and position of the heart were normal. Blotching of the lungs was attributed to recent pneumonia. The medical consultant diagnosed an inter-lobar empyema on the right side. Pus was not found on aspiration and an intercostal incision was made over the eighth interspace, without revealing pus in the pleural cavity. Two days later, the child's condition not having improved, the former incision was reopened and an exploring needle revealed pus beneath the diaphragm. Trans-pleural drainage was instituted, drainage was profuse, and the child gradually sank and died seven days later.

Probably the most interesting factor in this case was the fact that the subphrenic abscess was associated with the attack of pneumonia and arose apparently as an independent factor and not as the result of an empyema which had perforated the diaphragm. In this case the X-ray failed to demonstrate the condition, and our records show that in nine cases subphrenic abscess was recognized by X-ray before operation—in two it failed to do so, and in seven, for one reason or another pre-operative X-ray examination was not made, the condition probably not being suspected.

The question of the time interval between the original operation and the recognition of the subphrenic abscess varied considerably, and we were under the general impression that such abscesses usually make themselves manifest anywhere from two to three weeks after the original surgical interference. In this small series the earliest abscess was drained three weeks, and the longest period was eleven months after the primary operation, most of the cases falling between six and ten weeks.

In this respect there is, of course, the possibility that the condition existed earlier than the recorded time of its recognition, but if so, it was purely a question of failure to make a correct diagnosis. As evidence of the difficulty in this respect, in this series a correct pre-operative diagnosis was made in only seven instances; four times it was definitely wrong and



in seven it was not made at all, which latter group should be included in the mistakes, thus giving a percentage of thirty-eight correct—certainly nothing of which to be proud.

In this connection, and also demonstrating the fallacy of making a diagnosis of hysteria, the case of J. C. stands out quite vividly. He was a Hebrew of twenty-two, an actor by occupation, who, four weeks previous to his admission, noticed a swelling of his thigh. An abscess of the soft parts in this region was drained at this time. One week later he complained of severe pain over the right kidney, accompanied by sweating, without, however, presenting any other urinary symptoms. The history notes state that for years he had had symptoms of mild appendicitis. He was a poorly nourished man, examination being essentially normal aside from the fact that his liver was palpable about 3 centimetres below the costal margin, and he had a draining sinus in the right thigh. Aside from the palpable liver, there was neither mass, tenderness nor rigidity demonstrable in the abdomen. There was some tenderness over the right kidney without evidence of bulging or oedema. Temperature, pulse and respiration were 99°, 108, 28; leucocytes 30,500. Suspecting a perinephric abscess, an incision was made in the right loin and a normal-appearing kidney exposed. The abdomen was then opened through a right rectus incision and the liver was found to be considerably enlarged, extending halfway to the umbilicus and being smooth, tense and somewhat less firm than normal. The gall-bladder appeared to be normal and a chronic, somewhat adherent appendix was removed.

Two days later he still complained of pain in the right upper quadrant of his abdomen and it was at this time that it was suggested that he was probably of the hysterical type. Six days after his abdominal exploration an aspirating needle inserted through the eighth interspace revealed pus and resection of part of the eighth rib was immediately done. There was no pus in the pleural cavity, but it was obtained by aspirating through the diaphragm, revealing an unsuspected subphrenic abscess. He was drained and did splendidly for eight days—then developed pain in the left thorax, became quite toxic and died on the eleventh day after draining his abscess. A post-mortem was not obtained. This case is rather typical of those in which the diagnosis of subphrenic abscess was either wrong or not made.

In only one case was there the suggestion that an empyema had perforated the diaphragm and from a review of other recorded series this is comparatively a rare complication. Association of subphrenic abscess with disease of the biliary tract occurred in only two patients, one of whom presented some rather interesting features.

An Italian man of thirty-four gave a history quite typical of infectious cholelithiasis of twenty-two days' duration, being more acute for the twelve days preceding his admission to the medical wards—continuous upper right abdominal pain, daily vomiting, chills, fever, jaundice and leucocytosis. Except for jaundice, physical examination was essentially negative aside from the abdominal findings. He showed rigidity of the right rectus, slight generalized abdominal tenderness, liver not definitely palpable, spleen not palpable. He appeared quite toxic, and both Widal and blood culture were negative. Six days after admission abdominal exploration was done, revealing dense adhesions in the upper right quadrant, the gall-bladder being adherent to the gastro-colic omentum. The liver was quite normal and stones could not be palpated in the gall-bladder or ducts. The wall of the gall-bladder was apparently not much thickened and a cholecystostomy revealed only inspissated bile, pus not being present. The diagnosis was infectious cholangitis. He reacted fairly well from the operation and nine days later showed dullness and diminished breath sounds at the base of his right

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chest, accompanied by chills and free drainage from the gall-bladder. Three weeks later a subphrenic abscess was suspected and aspiration in the sixth intercostal space, mid-axillary line, obtained pus. Operation through the chest revealed foul, bile-stained pus coming from a walled-off tract which led inward toward the liver. The diaphragm had been markedly elevated, being above the incision (sixth interspace) and a hole was demonstrated leading from the pleura, through the diaphragm, to the liver. He reacted poorly and died three days later. Post-mortem revealed localized peritonitis about the abdominal incision and in the region of the gall-bladder. The small gut was firmly bound together in this region with the formation of an abscess directly beneath, in the retroperitoneal spaces. On breaking into this, a direct connection with the portal vein was found, leading from the abscess cavity directly into the liver. Many scattered abscesses were found throughout the liver. The gall-bladder showed no distinct changes aside from the operation. The chest contained a litre of fluid, and there was a hole in the diaphragm.

The pathologist was unable to demonstrate any area in the liver surface which would seem to indicate that there had been a rupture of a hepatic abscess, into the subphrenic region, and the infection of his upper abdomen probably resulted from leakage of infected bile into the peritoneal cavity by way of the drained gall-bladder, with subsequent formation of a subphrenic abscess which perforated his diaphragm. If this surmise be correct, it serves to emphasize one of the unfortunate complications which may attend drainage of the infected biliary tract, but the surgeon usually does not have much choice under such circumstances, drainage of the tract being requisite.

The question of surgical approach to the abscess varies with the suspected origin and location of the collection—thus when its source is retroperitoneal, *i.e.*, from a perinephric abscess, etc., we believe the best results will be obtained when the approach is from below the diaphragm. Should it be suspected that the abscess occupies one of the anterior suprahepatic spaces, presenting in the upper abdomen, the transabdominal route is preferably the method of choice. In most of the cases, however, presenting on the upper right aspect of the liver we believe that resection of the tenth or eleventh ribs with walling off of the pleural cavity from the drainage tract and direct drainage through the diaphragm, is the method of choice.

Reflection upward of the pleura in the costophrenic angle, with drainage from beneath this reflected pleura, is probably ideal if it can be accomplished, but it has been our experience that due to adhesions of these layers to the diaphragm and chest wall caused probably by the inflammatory reaction resulting from the abscess, this method is more theoretical than practical. Realizing the importance of preventing infection of an uninvolved pleura, we regard it as of the utmost importance to endeavor to avoid this by securing adhesions between the diaphragmatic and costal layers of the pleura by suture, pack, or both, when such adhesions are not already present. In but few instances will it be found that drainage is so urgent that a delay of a few days will not be warranted to accomplish this walling-off process.

In those cases where immediate evacuation of pus seems indicated, after suturing the two layers of pleura a sufficient amount of pus can be aspirated to relieve the toxic symptoms and tide the patient over the short period necessary to secure firm adhesions and protection of the pleura.

There were eight deaths in this group, a mortality of 44.4 per cent., which is about the average of other recorded series.

In addition to those fatalities already enumerated, a woman of sixty, following cholecystostomy with removal of stones, developed pneumonia sixteen days after operation, went on to empyema, the pus being of colon origin. This was drained and her original abdominal incision was reopened three weeks after the original operation, and 250 cubic centimetres of foul yellow pus removed. She did fairly well and then died suddenly four weeks later from acute cardiac dilatation. Post-mortem revealed the undiagnosed subphrenic abscess, her pleura having cleared up quite well.

A second case, as the result of a draining appendectomy sinus of one year's duration, showed at post-mortem abscesses of the spleen and left lobe of the liver, in addition to a subphrenic one on the left side.

The seventh case was a man of sixty-four suffering from an annular carcinoma of the sigmoid, whose long period of digestive troubles was attributed by the internist to hysteria (and this in 1924) when the röntgenologist stated that there was no evidence of an intestinal lesion nor gall-stones. The colon was slow in emptying without, however, signs of obstruction being present. This was in April, and three months later a cæcostomy was done to relieve his intestinal obstruction. Leakage occurred, from which he developed a subphrenic abscess and he died. Among the interesting facts brought out in the case was the failure to recognize an early carcinoma of the sigmoid, and again the danger of attributing symptoms to hysteria merely because the underlying pathological condition has not been ascertained.

A colored boy of seventeen was admitted to the hospital in April, 1930, with a diagnosis of appendiceal abscess. In 1927 he had been operated upon for a right perirenal abscess, pus not being found at the time of operation but subsequently draining from the wound eight days later, to be followed by a right empyema thoracis, which was drained by rib resection.

The next year he was admitted for pneumonia, and pleurisy with effusion, which did not require drainage.

Operation in 1930 revealed an acute appendicular abscess extending in the loin to the site of the old operative scar of his former kidney exposure, suggesting that the former perirenal abscess was due to a perforated appendix and not to any renal involvement. Drainage through his appendectomy incision was not satisfactory and three weeks later through and through drainage to the loin was established. He developed metastatic abscesses of the abdominal wall and right thigh. Six weeks after his appendectomy signs of subphrenic abscess appeared which cleared up, only to reappear three weeks later. At this time aspiration in the eighth interspace revealed a collection of turbid fluid beneath the diaphragm, which was drained through the diaphragm, a portion of the eighth rib being resected in the mid-axillary line. Four hundred cubic centimetres of fluid were removed, which proved to be sterile on culture, and continued so in spite of a faecal fistula developing through the appendectomy wound, the latter due probably to the bowel being perforated in exploring for a pus collection in the abdomen. In three weeks the drainage from the subphrenic abscess had ceased, the faecal fistula continuing.

The boy presented other features of interest, such as an acute post-operative psychosis, small pulmonary embolism, and acute nephritis, and he gradually wasted away and died a little over five months after his admission.

The X-ray showed the collection beneath the diaphragm, and the laboratory reported an acute suppurative appendix. Four blood cultures were negative.

Post-mortem failed to reveal any evidence of tuberculosis. It showed an old inflammatory condition which obliterated the right pleural cavity and evidence of a healed subphrenic abscess. A faecal fistula was present and a walled-off collection of pus in his pelvis, the abdomen being uninvolved.

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The above series is of course too small to warrant any conclusions, but among the facts which have impressed themselves may be mentioned:

1. One of the most frequent causes for failing to detect a subphrenic abscess is failure to consider its existence, and in this connection one should bear in mind that quite a fair proportion of these abscesses arise from causes other than infection within the abdomen.

2. The difficulties often encountered in arriving at a correct diagnosis.

3. One should not hesitate to use an exploring needle when circumstances warrant it and a correct diagnosis cannot be made by other means (physical examination and X-ray).

4. That the X-ray, while a great aid in establishing a diagnosis of subphrenic abscess, is by no means infallible.

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# THE MANAGEMENT OF PATIENTS WITH GASTRIC AND DUODENAL ULCERS\*

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A GREAT deal has been written about the medical versus the surgical treatment of patients with gastric and duodenal ulcers, with a high percentage of cases failing to get relief from symptoms after each type of treatment. It is not the purpose of this paper to lay down dogmatic rules for the treatment of ulcers but to say that both medical and surgical methods have their place in certain stages of the disease.

*Etiology.*—As in the case of any other disease, for example, cancer, until we find the causative agent, or agents, our treatment is more or less palliative whether it be medical or surgical. Infection seems to play a very important rôle and Saunders<sup>6</sup> has recently isolated from excised ulcers an alpha streptococcus of the non-hæmolytic type which seems to have a definite bearing on the cause of the disease. There are probably other factors, such as vitamine deficiency, and this is illustrated by Holt<sup>4</sup> and Veeder<sup>7</sup> in their reports on cases of ulcers occurring in infancy. These were usually found before the sixth month and in marasmic infants with a general lowered vitality. Whether acidity is a causative factor in the disease or results from the disease is far from settled, but our laboratory work does not always reveal hyperacidity in cases of proven ulcers. It would seem that hyperacidity is an incidental finding in the disease and bears no etiological relationship.

Our primary interest as clinicians, whether we be internists or surgeons, is to cure the disease or at least to relieve the patient of his symptoms. We do not consider ulcers a simple medical or surgical condition but one in which both methods of treatment may have to be used. It is essential to remember that a patient with an ulcer has a chronic recurring disease characterized by attacks of pain which occur at irregular intervals. The intervals between attacks may be from a few weeks to several months, and at times years.

In the Gastroenterological Clinic of the Fourth Medical and Surgical Divisions of Bellevue Hospital from January, 1928, to April 1, 1930, there were 238 ulcers under observation. Of this number thirty-nine have been operated upon for acute perforations and forty-four for chronic ulcers, leaving 155 unoperated ulcers. Of the unoperated cases there were 124 duodenal ulcers, fifteen gastric ulcers, twelve pyloric ulcers and four double ulcers, meaning the patient had lesions in both the stomach and duodenum. Our object has been to relieve the patient of symptoms and, if possible, to cure the disease by medical care, employing surgery only as a means of last resort.

The patients, on entering the clinic, are referred for X-rays of their teeth

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\* Read before the Delaware County Medical Society, Delhi, New York, June 10, 1930.

and extractions are done if necessary. If there is an indication of sinus or throat infection they are referred for X-rays and examination. A gastric analysis, complete blood count, Wassermann, urine and blood chemistry for urea nitrogen, creatinine, sugar, chlorides, calcium and phosphorus determination is done. In bleeding cases blood-platelets, bleeding and clotting, and clot retraction time is done. X-rays of the gastro-intestinal tract are done at frequent intervals.

The dangers from an ulcer are: first, perforation; second, hæmorrhage; third, carcinomatous degeneration. Perforation is a real danger and patients may perforate more than once and even after they have been under prolonged medical care and are apparently progressing satisfactorily. In a recent paper<sup>3</sup> read before the American Gastroenterological Association in which 105 cases of acute perforated ulcers were reported, there was noted an increase in the incidence during the past few years. In 1911, there was one case, as against thirteen for 1929. Also, six cases have occurred during the past two years while under medical care in our clinic. The only means of preventing this complication is to find the cause of the disease. Saunders,<sup>6</sup> by his agglutination test, seems to be in a position to aid in the diagnosis and to prognosticate the course of the disease.

Hæmorrhage is an alarming complication of ulcers. Gastric hæmorrhage will at times prove fatal in spite of every effort to save the patient by transfusions and conservative measures. There have been fifty-two cases of bleeding ulcers admitted to the Fourth Surgical Division since 1911, with six deaths in cases not operated upon but treated conservatively. It is interesting to note that these severe hæmorrhages occur in patients with a negative gastric history and the first warning is profuse bleeding. The chronic recurring hæmorrhages do not prove fatal and should have every chance of medical care, although we have had six cases of hæmorrhage occur in the clinic in patients under medical management that were progressing satisfactorily, but these cases have been controlled by transfusions and rest. There are also four cases that have been operated upon for bleeding ulcers which have continued to bleed. The operations varied from gastrectomies to gastroenterostomies and pyloroplasties. The best procedure is to treat the case conservatively, but if it continues to bleed over a long period, an operation should be performed and the ulcer cauterized or excised, plus whatever other procedure may seem advisable.

Carcinomatous degeneration may occur in gastric ulcers but it never occurs in duodenal lesions. Granting that it does occur in gastric lesions it is doubtful if the percentage is as high as some clinics estimate. MacCarty<sup>5</sup> has stated that about 70 per cent. of chronic gastric ulcers present cells of the cytologic appearance of cancer. Ewing<sup>2</sup> puts the incidence around 2 per cent. It is difficult to believe that the incidence of carcinomatous degeneration of gastric ulcers exceeds 10 per cent. If one employs gastrectomies routinely in cases of gastric lesions, the mortality will be at least 15 per cent. It is interesting to note that Balfour,<sup>1</sup> in his report on surgery of the stomach

and duodenum in the Mayo Clinic for 1929, operated upon 125 gastric ulcers. Of this number approximately 40 per cent. had partial gastrectomies; 35 per cent. excision with cautery or knife and gastroenterostomy; and 15 per cent. gastroenterostomy alone. We do not consider a gastric ulcer an operative case unless it fails to respond to medical care. An early gastric lesion responds to medical management more favorably than a duodenal ulcer.

*Treatment.*—All ulcers are considered as inflammatory lesions, regardless of location, and are treated by medical care, and surgery is resorted to if the case does not improve. An early carcinoma with an ulcerative area might be mistaken for a gastric ulcer but these cases do not respond to medical treatment.

The patients are treated in one of three ways: (1) ambulatory Sippy diet; (2) vitamins, vaccines and bland diet; (3) surgery.

That the ambulatory Sippy treatment has a definite place in cases of ulcer seems certain. Doctor Bishop supervises the ambulatory cases and will report on his results at a later date, but so far this method of management has given good results in most instances. Patients can remain on a strict milk-and-cream diet for several weeks, if they are not doing laborious work, and continue at their occupation without any hardship. Even though the patient can receive free hospital care for four to six weeks, due to economic problems at home, he does not get the mental rest which is essential in these cases. Doctor Hartung is using vaccines and vitamins on another group with some very satisfactory results. He has some early cases that have not been treated by other methods, and others that have failed to receive relief from symptoms after a Sippy diet, or following operations of different types. These cases are at times changed from one type of medical treatment to another. Doctor Hartung will report in detail on his work at a later date.

*Surgery.*—It has been our intention to operate on cases as a last resort only and so far we have had but five operations in chronic ulcers that we have treated. It is not our intention to state whether pyloroplasties, gastroenterostomies or partial gastrectomies should be performed, but we have cases under observation that were failures in all three types of operation that have been done in other institutions. The indications for operation, such as pyloric obstruction, long history with previous treatment, recurring hæmorrhage and gastric ulcers have been ignored, and all of these cases have received medical care before considering operation. The cases that have been operated upon so far have progressed very satisfactorily and most of them have had conservative types of operation, such as pyloroplasties or gastroenterostomies. If the cases are given a chance of medical management, the results from surgery in the medical failures would seem to be very gratifying.

#### SUMMARY

No conclusions can be drawn at present, but if one approaches this problem with an open mind, he will see some of the most startling results from both medical and surgical treatment in cases in which a good result is

least expected. Also, failures are encountered with both methods of treatment when we had every expectation of a good result. A patient cannot be considered cured until kept under observation for a ten-year period, whether medical or surgical treatment is advocated.

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# DUODENO-JEJUNOSTOMY AS A SUBSTITUTE FOR GASTRO-ENTEROSTOMY IN CERTAIN CASES OF DUODENAL AND GASTRIC ULCER AND APPARENT OBSTRUCTION OF THE STOMACH

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THE operation of duodeno-jejunostomy, an anastomosis between the first loop of the jejunum and the third, or the second portion of the duodenum, and for the purpose of regularly emptying the duodenum above a stenosis located at its lower part, has been widely popularized through the journals and Quain's<sup>1</sup> monograph on the duodenum. The brilliant results of recent duodeno-jejunostomy in chronic or recurring duodenal obstruction have been amply proven by case reports in the literature.

Sloan<sup>3</sup> proved the presence of periduodenal adhesions by operation in 362 cases and found a co-existing duodenal or pyloric ulcer fifty-two times. From these observations he concludes that partial duodenal obstruction at the duodeno-jejunal angle is sometimes the cause of duodenal ulcer or that it creates conditions favorable for ulcer formation. He obtained several cures of the ulcer by simple removal of the obstruction without gastroenterostomy. Kellogg<sup>4</sup> and I observed five cases of duodenal ulcer with duodenal stasis. In six cases the ulcer was active; in two of Kellogg's and one of Quain's, stenosing in Wilkie's. Wilkie reported a perforated duodenal ulcer. In a case of Deaver there were four perforations, with three operations of suturing and recovery, but death after fourth perforation. The autopsy showed an unsuspected obstruction of the duodenum above the mesenteric artery. Wilkie<sup>5</sup> again reported three cases, Higgins<sup>6</sup> five cases of duodenal ulcer as complications in duodenal stasis, and Barling<sup>7</sup> and Zoepffel<sup>8</sup> five and two cases respectively of gastric ulcer accompanying duodenal obstruction. Lane<sup>9</sup> restated his theory that duodenal stasis may produce either ulcer of the duodenum or stomach. Berg, Melaney and Jobling,<sup>10</sup> in their experimental studies after the production of a lasting duodenal obstruction with dilatation above and confirmed by fluoroscopic examination, noted, as well, an enormous increase in bacterial flora, mostly in the bacilli of the colon group.

Gastric retention and dilatation of varying degree is not uncommon, along with duodenal stasis, and has been noted by most writers on the subject. In a case of Stavely's and Wilkie's the gaping pylorus admitted several fingers. Moynihan<sup>11</sup> has pointed out that duodenal obstruction is a cause of the so-called "vicious circle" and Wilkie also stresses this point, as well as the point that recurrent symptoms after gastroenterostomy are due to unrecognized duodenal obstruction at the time of operation. Zoepffel likewise attributes some bad results after Billroth No. I to the fact that stenosis of the third portion of the duodenum had been unrecognized.

Quain makes the significant remark that it is, therefore, necessary always to verify the condition of the duodenum when a gastroenterostomy is made for gastric or duodenal ulcer.

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CASE I.—A man, aged thirty-five, with typical symptoms of duodenal ulcer, who, in spite of irregular Sippy and antacid diet, belladonna and alkalies, had profuse vomiting of blood, improved and hæmorrhage ceased after medical treatment. Filling defect persisted. (Case I, Fig. 1) gastroenteroptosis and dilated duodenum. Finney pyloroplasty with resection of ulcer; pathological report of malignant ulcer (discredited), symptom-free for eighteen months, usual confusing shadow-graft following pyloroplasty. (Case I, Fig. 2.) Sudden recurrence of symptoms and acute perforation; perforation cauterized and closed, gastroenterostomy to relieve tension in duodenum; symptom-free for fourteen months; recurrence of pain in epigastrium and tenderness, ulcer at gastrojejunal anastomosis.

CASE II.—Woman, aged sixty-two, pain in epigastrium, occasional vomiting. Two X-ray series with barium enemata and visualization of gall-bladder, showed only gastroenteroptosis and moderately dilated duodenum. Improvement of short duration



FIG. 1.—Case I. Persistent ulcer after hæmorrhage, ulcer clearly visible and palpable at operation resected. Finney pyloroplasty.



FIG. 2.—Case I. After Finney pyloroplasty and resection of ulcer, dilatation of duodenum, recurrence of ulcer and perforation. Cauterization and closure of ulcer and gastroenterostomy. Recurrence of ulcer from stasis and tension likely prevented by duodenojejunosomy and resection of ulcer. Marginal ulcer after gastroenterostomy to be closed and duodenojejunosomy.

on belladonna, alkalies and antacid diet, attacks of pain in epigastrium recurred from time to time over a period of four months' observation, finally passed blood by bowel and vomited blood. X-ray study showed dilated and deformed duodenum. (Case II, Fig. 3.) At operation dilated duodenum, ulcer in second portion of duodenum, relieved of pain by gastroenterostomy for eight months to date. *Impression.*—Same relief of symptoms and likely more enduring comfort by duodeno-jejunosomy.

CASE III.—Man, aged forty-eight; weight, 106 pounds, loss of forty pounds in weight, pain in epigastrium, frequent attacks of nausea and voluminous vomiting, pale and weak. X-ray study showed dilated duodenum, dilated stomach with eleven hours' gastric retention. (Case III, Fig. 4.) At operation bands of adhesions at terminal duodenum and rolling and narrowing of duodenum, dilatation of proximal duodenum.

Duodenum liberated and anastomosis made between first loop of jejunum and infra-mesocolic duodenum. The patient never vomited again, was on a full diet in the course of three weeks and according to his own statement remains perfectly well with a weight of 160 pounds, eating what and when he wants. Now remains well for six years. A defect in cap shown in X-ray and diagnosed ulcer was not found at operation as a visible and palpable ulcer.

CASE IV.—Woman, aged thirty-two, thin, pale; frequent attacks of nausea and voluminous vomiting. X-rays showed moderately dilated duodenum and stomach, gastric retention for eleven hours. A gastroenterostomy was done. After operation there was frequent vomiting of large quantities of bile-stained fluid, so-called "vicious circle." The vomiting was relieved by elevating the foot of the bed. Vomiting frequently occurred during six months and there was no improvement. Repeated X-rays showed markedly dilated duodenum and stomach and prolonged gastric retention. (Case IV, Fig. 5.)



FIG. 3.—Case II. Deformed and dilated duodenum, ulcer found at operation in second portion of duodenum, bulging near cap an artefact after violent hæmorrhage. Two former X-ray studies negative. Relieved by gastroenterostomy. Stasis and tention in duodenum would have been better provided for by duodenojejunosotomy.



FIG. 4.—Case III. Duodenal obstruction by adhesions and rolling of terminal duodenum. Nitch in cap diagnosed ulcer, not visible and palpable at operation. Completely relieved for six years by duodenojejunosotomy.

Second operation the terminal duodenum was surrounded by adhesions and narrowed and the terminal loop jejunum used for gastroenterostomy carried to the left; made a sharp angle at the duodeno-jejunal junction. A duodeno-jejunosotomy was done. There was no more vomiting, a rapid gain in weight and marked relief but multiple neurotic complaints, such as irregularity of menstruation, pain in hips, *etc.* X-rays after duodeno-jejunosotomy showed stomach emptying in four hours and rapid passage into cæcum (Case IV, Fig. 6.)

CASE V.—Woman, aged forty-two, thin, pale; frequent attacks of voluminous vomiting. History of possible tuberculous peritonitis when a child, formerly had cholecystectomy. X-rays showed dilated stomach and duodenum with nine hours' gastric retention, gastroenteroptosis. At operation there were multiple bands at terminal duodenum, marked angulation at duodeno-jejunal angle, and membrane holding terminal duodenum

## DUODENO-JEJUNOSTOMY

and proximal jejunum together. At operation, that duodenum and stomach be surely relieved of obstruction, the duodeno-jejunal angle was liberated from bands and membranes and also from the ligament of Trietz and the anastomosis made between gastric antrum and the duodeno-jejunal junction. The patient improved, gained weight but soon had an occasional return of attacks of vomiting and some diarrhoea. The stomach and duodenum now empties about as fast as the barium meal can be given. (Case V, Fig. 7.) The gastric contents rapidly fill the small intestine and by rapid overloading, vomiting recurs. *Impression.*—At the operation a duodeno-jejunostomy would have sufficed. The question is now before us of taking down the gastroenterostomy and making a duodeno-jejunostomy.

CASE VI.—Woman, aged forty-two; attacks of pain in epigastrium as well as pain in right lower abdomen, profuse menstruation, vomiting, elevation of temperature and leucocytosis, negative urine. Poor result with enemata. Brought to hospital as acute



FIG. 5.—Case IV. Markedly dilated duodenum "vicious circle" after gastroenterostomy, due to adhesions and falling of jejunal loop to the right followed by persisted duodenal obstruction completely relieved by duodenojejunostomy at second operation.



FIG. 6.—Case IV. Rapidly emptying duodenum and stomach in Case IV. Fig. 5 after duodenojejunostomy.

abdominal case and diagnosis of ovarian cyst, was formerly operated on for tuberculous spine with bone graft and appendectomy. Abdomen flat, scar of former appendectomy, tenderness and definite resistance over cecal region, soft mass over right adnexa, small mass over left adnexa. *Diagnosis.*—Ovarian cysts right and left, partial intestinal obstruction. At operation ovarian cyst size of lemon on left side. Cæcum down in right side of pelvis, filled with soft doughy fecal matter, ascending colon adherent to peritoneum, at site of former appendectomy. Colon liberated from abdominal wall, enucleation of left ovarian cyst. Patient vomited after operation large quantities of bile-stained fluid, in spite of good results following enemata on the second and third days and continued to vomit in spite of the fact that the abdomen remained soft. After a large enema and turning the patient over on her abdomen with foot of bed elevated, there was a cessation of vomiting and a sudden movement of bowels filling the bed. The patient was sustained on salt solution and glucose given in frequent and large

quantities intravenously during her vomiting. By the fifth day she was entirely comfortable and taking food. *Impression.*—Duodenal arterio-mesenteric ileus ("acute dilatation of stomach"). Compare with Case IV, Figs. 5 and 6, and so-called "vicious circle" following gastroenterostomy.

CASE VII.—Woman, aged sixty-nine; indigestion and dyspepsia number of years, getting worse lately, loss of color and forty-two pounds in weight. Recently has been using stomach tube for washing out stomach on account of gastric distress. Vomited large quantity of blood, estimated at quart to quart and half and still passes tarry stools. Thin, pale, hæmoglobin 40 per cent., general examination negative, given blood transfusion. Tender over right upper abdomen, mass felt in right hypochondrium and epigastrium. X-rays show irregular mass in antrum. At operation in antrum and extending to pyloric ring irregular mass with puckering of gastric wall and adhesions, size of lemon, with cap-like crater located in anterior wall nearer greater



FIG. 7.—Case V. Gastroenterostomy between detached duodenojejunal junction and stomach in case of duodenal obstruction. Extremely rapidly emptying stomach, vomiting and colitis. Advised closure of gastroenterostomy duodenojejunosomy.



FIG. 8.—Case VII. Following resection of over half the stomach for carcinoma in woman sixty-nine years old, six years ago. Never vomited after operation, gained 42 pounds in weight. Eats full diet with absolute comfort. Stomach empties in 1 to 1½ hours. Compare with Fig. 7, Case V.

curvature. Part of corpus, antrum and first portion of duodenum resected and anastomosis of the Polya type done. Gross specimen showed ragged ulcer with indurated base and edges. Pathological report of ulcer with carcinomatous changes. There was never any vomiting after operation, patient left hospital in sixteen days on soft diet, reached full diet within two months and has been in good health and comfort for six years, since January 31, 1924. (Fig. 8.)

In six of the above cited seven cases, pain, vomiting and loss of weight were prominent in all of them. Cases I and II vomited large quantities of blood, and Case III occasionally a small amount of blood. Cases III, IV and V had numerous attacks of voluminous vomiting and showed prolonged gastric retention and considerable dilatation of the stomach. Persistent X-ray studies finally exhibited dilatation and deformity of the duodenum, and in

Cases I and II ulcer of the duodenum was found both by X-ray studies and at operation, but the ulcer diagnosed by X-rays in Case III was not found at operation. Case I had a recurrence of ulcer and perforation after pyloroplasty and resection of ulcer and was temporarily relieved by closure of perforation and gastroenterostomy, but later developed a marginal ulcer at the stoma of the gastroenterostomy. Case II showed ulcer in second portion of duodenum at operation and has been relieved by gastroenterostomy. It was suggested that duodeno-jejunostomy, followed by resection of the ulcer, would have been the operation of choice in Cases I and II, as was done with perfect result in Case III, to relieve stasis and tension in the duodenum, and would likely have prevented recurrence and perforation in Case I and secured more permanent result in Case II. Case V was overdone and the effect produced was that of combined gastroenterostomy and duodeno-jejunostomy; Case VII showed less rapid emptying of stomach after result and satisfactory X-ray study. Case IV was a failure after gastroenterostomy, had "vicious circle," and persisting duodenal obstruction. Both cases should have received a duodeno-jejunostomy alone at the first operation. Case VI developed the so-called "acute dilatation of the stomach" after operation in the lower abdomen and was immediately relieved by posture, as was Case IV. Duodenal obstruction, "vicious circle" and "acute dilatation of the stomach" are frequently one and the same thing.

May I insist that it is rather definitely and clearly pointed out by the above seven cases and remarks that the best results have been obtained, where the ulcer is resected and where the point of obstruction is searched for and found and proper relief of stasis and tension cared for, by the drainage of the upper into the lower portion of the gastro-intestinal canal at that particular location. This particular location of obstruction is frequently in the terminal duodenum and the logical site of anastomosis is between duodenum and jejunum.

It seems, according to Quain, that Petit in his thesis on the "Strangulation of the Duodenum at the Level of the Mesenteric Root" (Paris, No. 67, 1900), was the first to conceive the operation of duodeno-jejunostomy and to perform it on the cadaver. Baker, according to Wilkie, was the first to propose it, in 1906. Staveland, in 1908, put into practice the first transverse colic duodeno-jejunostomy on the living, for a chronic occlusion of the duodenum by the mesentery.

About half a century has elapsed since the foundation of gastric operations and yet hardly a single revolutionary method, except duodeno-jejunostomy, has been developed during that time. Technical modifications and improvements have been added but the principles of enlarging the pyloric orifice as laid down by Heineke-Mikulicz, the gastrojejunal anastomosis of Woelfler and the gastric resections of Billroth remain the basal procedures. It is likely that none of these operations or their modifications have more than a mechanical action beyond the removal of the growth and that no enduring physiological basis has been established beyond the drainage of the higher into the lower portion of the gastro-intestinal tract and that this prin-

ciple of relieving stasis satisfies all surgical requirements and yields, where clearly indicated, satisfactory results.

In making the above statement I have taken into full consideration the works of Alvarez, and his description of the motion pictures and of Cole's studies of "The Living Stomach and its Motor Phenomenon." I admit the importance of a knowledge of the complicated motor function of the stomach and duodenum, the secretory function and even the nerve supply, as well as the confusion in terminology, such as "duodenal cap" for pyloric cap and the proper location of corporic, pre-pyloric and post-pyloric ulcers. But when all is said, the surgeon's problem is centred on evacuation of the stomach and duodenum regardless of the procedure employed for the removal of the lesion.

The process of evacuation of the normal stomach is described by Cole as follows:

"The chyme in the stomach is moved along from one chamber to another by the progressive peristalsis, there being some intermingling of the chyme of the corpus with that of the antrum. The fluid chyme is squirted through the pyloric valve into the reservoir cap and separated from the rest of the chyme in the stomach. The fluid chyme is taken out of the top or distal end of the cap by a broad peristaltic wave which carries it through the duodenum and probably continues throughout the small intestine. The frequency and activity of this broad peristaltic wave is the fundamental phenomenon which governs gastric evacuation. Gastric tone only presses the chyme against the under surface of the cap. Progressive peristalsis, modified by systole and diastole, no matter how strong, only squirts the chyme through the lumen of the valve into the cap. The pyloric canal closes with a definite sphincteric action, but it is closed for such a very short period of the gastric cycle that it does not normally prevent gastric evacuation, and if anything it possibly accentuates it by squirting a small amount of chyme through into the cap when it contracts. The pyloric valve tends to retain the solid food in the antrum and to allow the more fluid content to be squirted through into the cap. But if all these are functioning normally and actively, unless there is a broad peristaltic wave to propel the chyme from the top of the cap and carry it through the duodenum in finger-like masses, functional gastric retention ensues. Therefore we must reiterate that the broad peristaltic wave in the duodenum is the fundamental phenomenon which controls gastric evacuation."

It becomes immediately evident that if the broad peristaltic wave in the duodenum takes place in its progressive fashion from cap through the duodeno-jejunal junction into the small intestine, this route must be ever patent and obstruction of the duodenum will not only be followed by stasis and increase in bacterial flora but will markedly disturb the whole gastric motor mechanism. This condition is actually observed in cases of duodenal obstruction where violent antiperistaltic waves are seen in the dilated duodenum, the pyloric canal stands wide open and antiperistaltic waves traverse the stomach as vomiting takes place, and duodeno-jejunostomy may completely relieve this condition and restore gastric motor function. The operation chosen for draining or evacuating the stomach should respect the motor function of the stomach and the selective action of the pyloric valve and should assure the patency of the terminal duodenum. This last condition, patency of the terminal duodenum, is the most important factor.

(Fig. 8, Case VII.) In this case, though of a necessity, cap, antrum and most of the corpus of the stomach were resected on account of cancer, with a patent duodenum, clinically the stomach functions perfectly and is shown satisfactorily by X-ray studies. Compare Fig. 7, Case V, where the chyme is hurled through the gastroenterostomy into the small intestine with such rapidity that the brunt of volume causes overfilling, antiperistalsis and vomiting. This emptying of the stomach more or less rapidly, has been in large part the fault in a considerable percentage of my cases where gastroenterostomy was done. In this case, as well as in Case IV, Figs. 5 and 6, duodeno-jejunosomy alone should have been the operation first done. Both cases now have duodeno-jejunosomy plus gastroenterostomy; the latter, with satisfactory result, and the former, a failure due to too rapid emptying of the stomach. Certainly duodeno-jejunosomy alone would have attained better results in both cases and at the same time retained the motor function of stomach and duodenum as described by Cole.<sup>12</sup> Likewise, duodeno-jejunosomy alone or duodeno-jejunosomy with resection of the ulcer would have relieved the stasis and tension in the duodenum, and hence bacterial growth, would have preserved the motor function of the stomach and duodenum in Cases I and II, Figs. 2 and 3, would likely have forestalled the recurrent ulcer and perforation and the marginal ulcer in Case I, would have secured the result in Case II, as was so brilliantly accomplished in Case III by duodeno-jejunosomy alone and at the same time would have preserved the motor function of stomach and duodenum, disturbed by gastroenterostomy.

Zoeppfel, quoted by Quain,<sup>1</sup> says that when a gastric ulcer and a stenosis of the third portion of the duodenum coëxist, Billroth No. II is indicated, a pylorotomy, and that Billroth No. I should be abandoned. This conclusion seems absolutely illogical, since with Billroth No. II, as well as with Billroth No. I, the duodenal retention will persist after operation. Whatever gastric operation is made it is indispensable to establish drainage for the chronic retention in the third portion of the duodenum.

The startling report of Cole<sup>13</sup> of twenty-six cases of gastric ulcer treated surgically and to be compared with thirty-six similar cases treated medically is indeed appalling:

"In the twenty-six cases presented, from verified records, eleven were treated with gastric resection, ten with excision and five with gastroenterostomy without excision. Of the eleven treated with gastric resection, six lived to leave the hospital and five died while in the hospital. Of the ten treated with excision; two were mucosal ulcers and one, as proved by microscopical examination, was already a healed ulcer. Of the remaining seven, two died, two were worse, one improved, and two were said to be improved, but in one of these, even with a special request for a röntgen-ray examination after the operation and before the patient left the hospital, such a procedure was not granted and we were unable to obtain further data. All of the three cases treated with gastroenterostomy lived but as we can compare each of these with a similar case treated medically without gastroenterostomy, the question arises: Did the ulcer heal because of the gastroenterostomy, or in spite of it?"



Compare this report with that embraced in a recent paper by Brenizer<sup>11</sup> where the various operations upon the stomach and duodenum are listed in 108 cases. This list embraced nine cases of gastric resection for gastric ulcer or cancer without a single death in less than a year's time and two deaths from metastasis. Gastric function remained satisfactory in all cases, even in spite of death from metastasis, equal to results in Case VII, Fig. 8. Every living case, seven cases in all, has presented large, visible, and palpable lesions at operation; has been verified by pathological section; has received an anastomosis of the Polya type; has a patent duodenum; and has been frequently seen or heard from during a period of ten years. However this question of operative indications and post-operative results may be, it still holds the "center of cyclonic controversy." This question is not pertinent to this paper except insofar as a failure to recognize an obstruction of the duodenum may prevent the success of an otherwise properly indicated and executed operation whether that operation be simple excision, pyloroplasty, gastroenterostomy or Billroth Nos. I and II. In these cases a combined duodeno-jejunostomy is the only logical operation, and, furthermore, it is a necessary operation. In selected cases of duodenal ulcer, and even gastric ulcer, of the gastroenteroptotic type of individual and with duodenal stasis, relief of tension and stasis can be directly attained and at the same time normal motor function of the stomach and duodenum preserved, by making the anastomosis, rather than between stomach and jejunum, preferable between duodenum and jejunum.

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# TRANSACTIONS

OF THE

## PHILADELPHIA ACADEMY OF SURGERY

STATED MEETING HELD JANUARY 5, 1931

The President, DR. GEORGE P. MULLER, in the Chair

CALVIN M. SMYTH, JR., M.D., Recorder

### TUBERCULOUS PERITONITIS AND RECURRENT UMBILICAL HERNIA

DR. GEORGE M. LAWS presented a patient to illustrate the repair of incisional hernia without removing the sac nor disturbing the viscero-parietal adhesions. A woman, aged fifty-nine years, was admitted to the Medical Ward of the Presbyterian Hospital, July, 1929, complaining of weakness, cough and enlargement of the abdomen. She had been operated upon for strangulation of an umbilical hernia in 1922, but noted recurrence four years later. Her medical history was unimportant thereafter until April, 1929, when she had an acute illness called congestion of the lungs. Since then she had not felt well and a month before admission the abdomen began to grow larger. She weighed 205 pounds; her enormously enlarged abdomen was symmetrical except in the mid-region which was the seat of a recurrent umbilical hernia. Movable dullness and a definite fluid wave were present. Peristalsis was hyperactive.

After two weeks' observation, during which the evening temperature rose to about 101° F., an operation was determined upon.

A transverse incision in the line of the abdominal scar revealed a thick-walled sac which was opened with the escape of a large quantity of dark brown fluid. The intestines, mesentery, liver and spleen were studded with small, white, hard nodules that were proven by biopsy to be tuberculous. The problem of dealing with the hernia then arose. Coils of small intestine were fused with the sac so firmly that herniorrhaphy in the usual way was impracticable. The wound in the sac was closed, the rupture was reduced *en bloc*, as it were, and the repair was completed by overlapping the fascia.

Recovery was complicated by left tuberculous pleural effusion which required aspiration thirty days after operation. The patient was discharged ten days later. She reported recently at the follow-up clinic that convalescence had been satisfactory and that she had remained free of symptoms. Examination showed no abdominal fluid and no hernia.

DR. GEORGE P. MULLER said that he had had occasion several times in the case of large incisional hernia below the umbilicus, to practise a method similar to the one described, without penetrating the peritoneal cavity. After dissecting out the skin scar the dissection is carried laterally until the edges of the anterior fascia have been identified. About one-half inch lateral from the edge of the retracted rectus muscle an incision is made from top to bottom in the anterior sheath. The median edge of this incision on either side is then sutured together in the median line to form a new linea alba, carrying the rectus muscle practically to its original position.

## PHILADELPHIA ACADEMY OF SURGERY

The lateral edges are then sutured together, if possible, still further, pulling the recti muscles together in the median line. If the latter suture is not possible the defect of fascia over the muscle is replaced by a fascia transplant from the thigh.

### PENDULOUS ABDOMEN—LIPECTOMY

DR. GEORGE M. LAWS reported the case of a woman with a pendulous abdomen from which he removed a segment that weighed twenty-four pounds.

When first examined, in February, 1928, she was twenty-eight years old



FIG. 1.—Pendulous abdomen. Lateral view.

FIG. 2.—Antero-posterior view.

and weighed 362 pounds. Standing, the abdominal wall dropped almost to her knees (Fig. 1), and walking, each step pushed half of the mass forward. The chief complaint was pain, evidently caused by the dragging weight.

A thorough examination had been made by a prominent internist, who found no endocrine disturbance. X-ray of skull, blood examinations, basal metabolism and sugar tolerance tests were all practically normal. She had been taking a gland preparation for a year but was still gaining weight. After seven months of dieting she had lost only eight pounds, and returned for operation chiefly because of the pain.

Operation October, 1928, at Presbyterian Hospital. A transverse bow-shaped incision was made through the skin and fat below the umbilicus,

## SUBPHRENIC ABSCESS

because the umbilicus supports these tissues. It was a long operation and the patient was somewhat shocked. Wound healing was primary, except where the tubes emerged and mild superficial secondary infection occurred at two of these places. Recovery and result were entirely satisfactory.

The wedge of tissue measured 37 inches from tip to tip, its greatest width was 14 inches, the average thickness 3 inches.

## SUBPHRENIC ABSCESS

DR. HENRY P. BROWN, JR., read a paper with the above title for which see page 1075.

DR. ELDRIDGE L. ELIASON said that he had treated eight such cases in the last seven years, although the essayist stated that he found but eighteen cases in two large hospitals, ten in twenty years in one and eight in the last eight years in another. As to the etiology the speaker remarked that in 1926 he reported twelve cases of liver abscess, ten of which were personal cases, all secondary to appendicitis, occurring from ten days to eleven months previously. In these twelve cases, seven had solitary right lobe abscess. Of these, five had proven subphrenic abscess also. Last week he discharged from the hospital another of the same type, making six in which the two abscesses existed in juxtaposition, as an hourglass cavity. It is well known that solitary liver abscess following appendicitis is probably embolic and that it has a predilection for the right lobe and tends to extend toward the upper surface of the liver. Only two of the above eight were near the under surface of the liver. It is reasonable to suppose that a subcapsular small abscess on the upper surface could also cause a subphrenic collection comparable to the supposed causation of an empyema thoracis following a pneumonia. Bile found in the subphrenic collections indicates this connection. Furthermore, in none of these personal cases was there any evidence of abdominal gutter extension. Another argument in favor of the liver origin is the fact that several of his cases as well as some of Doctor Brown's had no recent cause for the condition, the appendiceal attack or operation being as old as eleven months in one instance. Doctor Brown speaks of a possible thoracic origin only to cast possible doubt upon the same, and the speaker agrees with him entirely. In his liver and subphrenic abscess cases, the first diagnosis was suspected basal pneumonia, with lung changes shown clinically and by X-ray. Again, exploration by needles to the abscess by the Ochsner operation, which consists of the subperiosteal resection of the twelfth rib. In that way one gains entrance to the right posterior and the right interior space. The dissection is not difficult. By the hand one can differentiate the surface of the liver from the diaphragm and avoid any injury to the diaphragm proper; drainage is well maintained.

DR. HUBLEY R. OWEN said that in a case at the Women's College Hospital, which was operated upon about six weeks ago for a simple cholecystectomy, the patient when about to be discharged suddenly developed severe pain in the chest and a rise in temperature to 102-103°. There seemed to

be every sign of pleurisy at the base of the right lung. The chest was strapped but there seemed to be no improvement. A few days later an X-ray was taken which indicated that she had an abscess because of the elevation of the diaphragm. Recalling Doctor Eliason's report before the Academy, he opened the abdominal incision and found the liver and the region of the cholecystectomy normal, but the lower margin of the diaphragm was bulging. He went in above and removed about 500 cubic centimetres of fluid which in appearance resembled the fluid from a streptococcus empyema. The patient then made an uneventful recovery. He was very much confused as to the origin of this infection. It certainly did not appear to be from the abdomen and there were no findings in the chest to account for it. Accidentally puncturing the infected subphrenic area secondarily gives empyema. The presence of the colon bacillus argues for abdominal origin, although its absence is no proof against the same; colon pus was found in only one of his cases, the others being coccal. Of the other two cases in his personal series, one was due to an old perforated duodenal ulcer and the other to extension from an acute pancreatitis. These figures, therefore, indicate that appendicitis causing hepatic abscess is the most frequent cause of subphrenic abscess rather than that peritonitis causes it by extension up the flank or by the lymphatics.

Errors in diagnosis will be and are growing less frequent with the proficiency of X-ray reporting. The apparent increasing frequency is merely an increased accuracy in diagnosis and the decreasing mortality is due to the same. These patients no longer die with a suppositional typhoid fever or septic pneumonia.

DR. THOMAS SHALLOW mentioned as an additional fact pertaining to subphrenic abscess secondary phrenospasm, associated with much dilatation of the lower end of the oesophagus. He further emphasized that in diagnosis the X-ray is the most valuable method at our disposal. Of all the cases that he has seen every one that was diagnosed correctly was diagnosed by the use of the X-ray.

DR. BENJAMIN LIPSHUTZ remarked that he had had six cases of subphrenic abscess and in every instance he was able to gain access to the abscess by the Ochsner operation, the subperiosteal resection of the twelfth rib. In that way one gains entrance to the right posterior and the right inferior space. The dissection is not difficult. One can get his hand in and differentiate the surface of the liver from the diaphragm and avoid any injury to the diaphragm proper. Drainage is well maintained.

#### SURGICAL MANAGEMENT OF CRANIAL INJURIES

DR. J. STEWART RODMAN pronounced the Annual Oration as above entitled, for which see page 1017.

# TRANSACTIONS

OF THE

## NEW YORK SURGICAL SOCIETY

STATED MEETING HELD DECEMBER 10, 1930

The President, DR. EDWIN BEER, in the Chair

### ARTHROTOMY OF KNEE

DR. IRA COHEN presented a man fifty-five years old, who in December of last year was brought into Mount Sinai Hospital two hours after being struck by an automobile. He had a lateral dislocation of the left knee, the inner condyle of the femur was prominent and there was considerable abnormal mobility of the joint. The X-ray examination showed a subluxation with mesial displacement of the femur. An irregular shadow was seen overlying the joint space in the intercondylar area which was interpreted as a possible tear of the crucial ligament carrying with it part of the tibial insertion.

Under anæsthesia an attempt at reduction was made the same day and a plaster bandage applied. Reëxamination by the X-ray showed the subluxation to be almost but not entirely reduced, but a good antero-posterior view was not obtained. When the plaster was removed two weeks later, it was seen that a partial subluxation still existed. After another week the patient was allowed on crutches, and at the end of the next week he was referred to the physiotherapy department in the Out-Patient Department. He had very little pain and was able to get about with crutches; motion was limited to approximately thirty degrees.

When he reported at follow-up two months later the leg could not be completely extended at the knee and the motion was more limited than at time of discharge. A month later there was increased flexion deformity, hardly ten degrees of motion was present. There was no change in the Röntgen picture.

April 9, 1930, he was readmitted to the hospital and two days later operated upon. The joint was opened by a long incision on the mesial side of the patella, which was displaced laterally. The fixation of the joint seemed largely due to a piece of bone which was found to extend forward and mesially from the anterior crucial ligament to which it was intimately attached. After excision of this piece of bone the joint was closed. No splint was used and early motion of the joint was encouraged. X-ray examination showed the subluxation much improved and some of the bony shadows previously seen in the joint to be absent. The bone removed at operation was reported as showing chronic inflammation and fibrosis. The patient was discharged from the hospital a month after the operation. When seen a month later he was still using crutches. Four months later he still had some weakness of the knee, but there was about 75 per cent. normal function. It is now ten months since the operation, and he is able to carry on his work as a laborer.

### LATE ULNAR NEURITIS, FOLLOWING FRACTURE; TRANSPOSITION OF THE NERVE

DR. IRA COHEN presented a man now thirty-eight years of age, who was admitted last August to Mount Sinai Hospital with the following story:

Thirty-two years previously, at the age of six, he fell down a flight of stairs and sustained a fracture of the right elbow. Following this accident he had a deformity of the elbow but no limitation of motion. Two years before coming under observation he first noted numbness in the fifth finger. In the course of time this numbness spread on to the palm and dorsum of the hand. For about the same period of time he noted some weakness of the hand, and that the inner side of the palm of the hand was getting smaller.

On examination he showed some contracture of the fourth and fifth fingers of the right hand. There was atrophy of the hypothenar eminence and of the interossei. There was weakness in flexion of the fourth and fifth fingers with paralysis of abduction and adduction of the last four fingers. Sensation was much diminished over the fifth finger on both its palmar and dorsal aspect. The elbow showed a well-marked deformity, Röntgen examination of which disclosed an old ununited fracture of the external condyle of the humerus.

August 8, under local anæsthesia, the ulnar nerve was exposed on the posterior aspect of the elbow. It was swollen to about three times its normal size and was a deep pink in contrast to the normal color above and below. It felt firm and infiltrated. It was freed from its bed and transposed to the anterior aspect of the joint where it was held by a sling of fascia made from the deep aponeurosis. He was discharged eleven days after the operation. He was seen five weeks later at which time there was a considerable return of power and complete return of sensation. Now five months after operation he still has marked atrophy, but power is improving.

#### EPITHELIOMA OF GLANS PENIS

DR. KIRBY DWIGHT presented a man, fifty-four years of age, who entered Roosevelt Hospital in May, 1929, with the following history: About six months ago, he noticed a small nodule on the glans penis near the meatus, together with considerable œdema of the prepuce. A few weeks later the nodule broke down. Since that time, there has been a progressive ulceration and erosion of the entire glans and an increasing œdema of the anterior half of the prepuce. He has also had moderate pain in the right groin, but has not noticed swellings in either inguinal region. There is no venereal history. There was marked œdema of the entire penis. There was a deep, irregular ulceration which had destroyed about half of the glans. The edges of the ulcer were raised and hard. A yellowish, purulent exudation could be expressed from several small sinuses. There was infiltration of the entire glans, and of the corpus spongiosum for about 2 inches. The prepuce also was involved. The right inguinal lymph nodes were moderately enlarged and moderately tender. On the left side they were slightly enlarged but not tender. A microscopical examination of a small section removed from the edge of the ulcer confirmed the diagnosis of epidermoid carcinoma, and a few days later a complete amputation was done.

Using gas-ether anæsthesia, a block dissection was made of the inguinal and femoral lymph nodes, cleaning out the inguinal canals and removing the spermatic cords and testes. Then the patient was placed in the lithotomy position. The incision was carried around the base of the penis and down the anterior median raphe of the scrotum. The urethra and corpus spongiosum were divided well away from the cancerous infiltration, about an inch and a half distal to the bulb. Then the corpora cavernosa were dissected well back to the crura, where they were divided and the stumps closed with catgut sutures. An opening was made in the median raphe of

## CARCINOMA OF THE RECTUM

the scrotum posteriorly, and the stump of the urethra, after being split on its posterior side for about half an inch, was sutured to this opening. A catheter was introduced and held in place by suture.

Pathological examination of the specimen showed that the line of amputation was well away from the growth. The lymph nodes were found to be hyperplastic but no metastatic tumor cells were found in them. The wounds healed with only a slight infection in the right inguinal region. There was no difficulty in urination and the patient was discharged on the forty-third day.

At the last examination two weeks ago no evidence of recurrence or metastasis was found. At the time of the operation, it was hoped that the patient would be able to urinate standing up without soiling his clothes, but it has turned out that the stump of the urethra is too short to permit it.

## CARCINOMA OF THE RECTUM

DR. KIRBY DWIGHT presented a man, aged thirty-one years, who entered Lincoln Hospital in November, 1929, on account of obscure rectal symptoms from which he had been suffering for about one year. On rectal examination, a firm, smooth, projecting, ring-like mass was found about 1 inch beyond the internal sphincter and extending up along the rectum.

A biopsy was done and the diagnosis of colloid carcinoma was made by the pathologist. As soon as the pathological report was received, an exploratory coeliotomy was done. The growth was found to be confined to the rectum, not infiltrating the bladder nor adherent to the walls of the pelvis. A few small, hard lymph nodes were felt in the lower part of the meso-sigmoid, close to the bowel. No signs of metastasis in the liver. The large intestine was not dilated nor appreciably hypertrophied. The meso-sigmoid was very short. A left intramuscular incision was made and a permanent colostomy was made following the method of Dr. Charles Mayo. This was done under spinal anæsthesia.

The loop of the sigmoid was opened on the third day and divided on the eighth.

Sixteen days after the colostomy the rectum was removed under spinal anæsthesia. The posterior route was employed, with the patient in the flexed prone position. The gut was amputated a little above the recto-sigmoid junction and the stump of the sigmoid was inverted and closed, and then sutured to the pelvic peritoneum as the opening into the peritoneal cavity was being closed.

The patient was transfused two days before the resection and again ten days after it, 500 cubic centimetres of blood being given each time.

Recovery was without incident except that the plastic work on the colostomy became infected and an extra opening appeared in the angle made by the proximal loop of gut as it entered the subcutaneous tissue. This opening was closed and has remained closed.

The patient now feels well and has gained a good deal in weight. He keeps himself slightly constipated and has no trouble or annoyance from the colostomy. He wears a pad merely as a safeguard. He has not found it necessary to use pressure over the subcutaneous channel of the stoma. He is, however, considerably annoyed by the distal loop of the colostomy. It prolapses about 10 to 12 centimetres when he stands upright. When it is reduced, he has a colicky pain for a few moments. This prolapse is evidently not a result of peristalsis but a hernial protrusion caused by intra-abdominal pressure. The cause of this protrusion, in this particular case, may be the



short meso-sigmoid, previously mentioned. It prevented the pulling down of as much of the sigmoid as usual at the time of the resection of the rectum. It is planned to re-operate and either to remove the entire distal segment or to resect merely the redundant portion of it.

DR. SEWARD ERDMAN said that Doctor Dwight's explanation of the technic used in attempting a certain degree of control of the artificial anus brought up the question whether any attempts at control by plastic operations are worth while. If the colostomy is conveniently placed and the patient is trained to care for it by adhering to a dry diet and administering a small enema each morning through the colostomy opening, he can establish regular habits and go through the rest of the twenty-four hours without troublesome soiling. The main point Doctor Erdman wished to emphasize was that operations for cancer of the rectum are accompanied by very high mortality and the whole question has not yet been settled as to whether the one-stage or the two-stage method should best be employed. Jones, of Boston, has had excellent results using the one-stage, but Lahey has recently pointed out a logical objection to any one-stage abdomino-perineal operation: namely that if you leave the gut closed you inflict on a patient suffering from the shock of a big operation the additional strain of leaving him with a closed gut. You are therefore causing artificial intestinal obstruction on top of a huge dissecting operation. Doctor Erdman believed that some form of two-stage operation, establishing a colostomy first, was probably the safer method of attacking cancer of the rectum.

DOCTOR DWIGHT agreed with Doctor Erdman in his observation that as a rule plastic work does not help much in the control. Any opening of the gut without a real sphincter is going to be incontinent, unless the patient can make the bowels moderately constipated. In this type of operation, however, leaving in the upper part of the sigmoid, the plastic has value in that the two stomata are separated by normal skin, and a cup can be applied to the proximal stoma without including the distal one. Thus intestinal contents will not pass into the blind distal loop.

#### CANCER OF THE LARYNX

DR. GEORGE H. SEMKEN presented the following patients:

CASE I.—*Extrinsic Cancer of the Larynx with Early Lymph-node Metastasis.* R. E. McK., aged fifty-one years, a bank clerk, came under observation February 25, 1929. Four months previously, he had noticed a slight sticking sensation on the left side of the throat, during swallowing. This had remained relatively stationary for four to six weeks, then became more noticeable and had progressed continuously since that time. Two months ago, his physician found a small ulcer in the region of the left arytenoid with relatively considerable swelling in the surrounding area. This was considered an inflammatory process, and several applications of some silver solution were made—nineteen in all—during the following two months. There was some pain after the treatments, but this has not been pronounced. There have been no other symptoms beyond an occasional slight "hack"; and there has been no disturbance in speech.

The family and personal histories contained no relevant data. There had been no known antecedent cases of cancer and no severe previous illness. Venereal disease was denied, and the patient's Wassermann reaction had been negative. He seldom drank alcoholic liquors, smoked about three cigarettes during the day and two pipes in the evening, and had no unusual occupational factors of throat irritation. His general health was good.

Laryngoscopic examination showed cancer in the left pyriform sinus with extension to the edge of the epiglottis, to the aryepiglottic fold and the arytenoid, and to the lateral wall of the hypopharynx. There was a central excavation approximately 1.0 by 0.5 centimetre in surface diameter. The adjacent regions were hyperæmic and slightly œdematous. The vocal cords and the remainder of the larynx were normal. Upon digital examination, the carcinoma was found to be a stony hard tumor mass, approximately 1.5 to 2.0 centimetres in diameter. It extended to the wall of the hypopharynx but was not yet fixed. In the regional lymph nodes of the neck, there was one enlarged, firm node 2.0 by 1.5 centimetres in diameter, in the left carotid packet, and a smaller, softer node on the right side.

March 5, 1929, a radical laryngectomy was done with the removal of part of the lateral wall of the hypopharynx, well away from the tumor, and the removal, in block, of the related deep cervical lymphatics on each side, from the jugular fossa down to the omohyoid crossing. Colonic oil-ether anæsthesia. The tracheal mucosa was anæsthetized with a small quantity of novocaine 4 per cent. solution, injected into the lumen through a fine needle puncture between two tracheal rings. The trachea was divided transversely, between the cricoid cartilage and the first ring. The trachea was next carefully separated from the œsophagus, drawn into the transverse episternal incision, and sutured into place there with interrupted silk sutures. Four of these, at the main compass points, passed wholly around the first tracheal ring, to unite the trachea firmly to the skin (but they were not tied tightly enough to produce necrosis). The mucosa of the trachea was carefully sutured to the skin with interrupted fine silk sutures. The trachea was thus protected against the danger of aspiration of blood from the further operative procedure.

The skeletonizing of the larynx was now completed by the ligation and division of the remaining inferior and superior vessels respectively, the division of the nerves, and the clearing of the inferior constrictor muscle. A strong suture was inserted around the cricoid cartilage anteriorly, to serve in gently raising the larynx from its bed, and the larynx was dissected free along its posterior attachment, through the lower half of this extent. The wound field was then well protected with moist gauze compresses. The hypopharynx was opened on the uninvaded right side by a vertical incision in the lateral wall, through the inferior constrictor and the hyothyroid membrane. This incision was prolonged at its upper end by a curve mesad, below the hyoid bone, and the tumor region was brought well into view. The hypopharynx was cleansed with a 2 per cent. lysol solution on gauze wipes, and with alcohol; and the final excision was made with curved scissors, (1) across the root of the tongue, (2) across the hypopharynx well below the arytenoids, and (3) widely around the site of the tumor. An Einhorn tube with the Rehfuß tip was passed into the stomach through the opening in the hypopharynx; and the distal end was carried, *via* a catheter, through the pharynx and out of the nose. The large opening in the hypopharynx was completely closed in a Y-shaped line of suture, with interrupted chromic gut in two layers; the anterior edge of each sternocleidomastoid was brought across the large vessels of the respective sides, and sutured to the posterior

digastric above and to the deep fascia below, thus completely separating the vessels and the posterior spaces from the anterior part of the wound, where leakage and infection might occur. Similarly, the space behind the trachea (leading to the mediastinum) was closed with a few chromic gut sutures. The flaps of skin and platysma were brought into alignment and sutured with silk. Drainage was provided (1) at the lowest angle of each closed-off posterior space, (2) at the respective ends of the upper incision, and (3) at the lower end of the mid-line incision. The ends of the sutures at the tracheal opening, left about 4 centimetres long, were fastened to the skin with adhesive strips and the sutures were greased with vaseline (to prevent crust formation).

The patient was returned to bed in good condition and had a relatively normal convalescence. A small accumulation of fluid on the left side required a separate small incision and drainage; and there was a slight leakage of mucus at the mid-line for a time; but otherwise, the wounds healed well. The Einhorn tube was removed on April 15. The microscopical examination of the removed tissue showed squamous-celled epithelioma of the larynx, grade B, with metastasis to the regional lymph node in the carotid packet.

There has been no demonstrable recurrence, one year and eight and a half months after operation. He has had no difficulty in swallowing solid food, and his general health is excellent; but he has not yet learned to speak above a whisper, and does not use the artificial larynx.

CASE II.—*Advanced Mixed Cancer of the Larynx [Intrinsic and Extrinsic]. Laryngectomy with Limited Lymph-node Removal. Recurrence in the Lymph Nodes. Apparent Cure, Two Years and Eleven Months.* Wm. F., aged sixty-six years, a tailor, came under observation September 28, 1925. He had had a cough from chronic bronchitis for many years, and ascribed to this cause also, a hoarseness that began ten months previously. The hoarseness had been progressive and the breathing had been slightly stridulous in the preceding three weeks. There was moderate cough with thick, yellow expectoration. There had been no other symptoms. For a number of months, he had been treated for a "cold." Seven months previously, the diagnosis of cancer had been made by a laryngologist and operation had been advised; but he had consulted another laryngologist, who had treated him with local applications instead, for about six months. The family history was negative for antecedent cancer cases. He had had no previous illness of importance. He seldom took alcoholic liquors; but he had been a continued smoker (cigarettes, cigars or pipe). His general health, apart from the chronic bronchitis, had been good.

Laryngoscopic examination showed a cancerous mass that filled the left half of the cavity of the larynx and had crossed anteriorly to invade the right side also. The site of origin had apparently been in the anterior part of the left ventricular fold, with extension mainly downward into the larynx and forward across the anterior commissure. The growth had also been expansile, and the resultant tumor was an irregularly rounded, smooth mass, red in color with yellowish areas in places where the underlying cancer had thinned out the mucosa. There was apparently no lateral extension, but subsequent examination of the tumor showed invasion of the epiglottis and the left aryepiglottic fold. No enlarged cervical lymph nodes were palpable.

The operation, October 1, 1925, consisted in the removal of the larynx in block with the anterior nodes of the deep chain on the left side, which were considered immediately regional to the process. At the conclusion of the operation, a gastrostomy, by Kader's method, was also done. The procedure followed the plan outlined for the previous case, with the implantation

of the trachea in a separate episternal opening; but with the dissection of the lymphatics limited to the node groups anterior to the internal jugular vein. Convalescence was normal. There was no leakage from the pharynx and the wounds healed *per primam*. Liquids were given by mouth on the eleventh day; and the gastrostomy tube was removed on the twenty-fifth day. The gastrostomy closed promptly and this wound was completely healed ten days later. Microscopical examination of the tumor showed squamous-celled cancer.

The date of appearance of the (recurrent) lymph-node tumor in the neck is uncertain, because the patient did not report regularly for the follow-up examinations. December 30, 1926, fifteen months after operation, he had an ellipsoid mass in the upper part of the left side of the neck, 5 by 4 centimetres in diameter, in the region of the superior group of the deep chain. He had noticed this only two weeks previously; and that region had been slightly painful for the preceding few days. There was no evidence of local recurrence; and no enlarged nodes were palpable elsewhere in the neck.

The second operation, January 3, 1927, consisted in the removal of the deep lymphatic structures of the left side of the neck from the jugular fossa to the clavicle, together with a large part of the internal jugular vein and the anterior part of the sternocleidomastoid muscle. The vein had been almost completely occluded by the pressure of the adherent tumor and the muscle had been invaded. Convalescence was uneventful. One month later, there was moderate swelling in the middle zone of the neck which did not disappear. It gave the impression of an inflammatory process, but it was deemed advisable to give deep X-ray therapy to that region, and this has been done. There is still a definite area of thickening, apparently from fibrosis; but there is no evidence of a recurrence of his cancer.

CASE III.—*Intrinsic Cancer of the Larynx—Three-Year Result.* L. S., aged sixty-eight years, came under observation October 10, 1927. A slight hoarseness had been noted ten months previously, and this had continued without appreciable increase until the preceding few weeks. There had been no other symptoms except a moderate increase in mucus. He had been under the care of a laryngologist since the onset, who found a "granuloma" in June; but there had been no active treatment. The condition had been recognized as cancer by a second laryngologist a few days previously. The family history was negative for antecedent cancer cases, and there had been no previous illness of importance. He did not drink alcoholic liquors; but smoked four or five cigars daily and, infrequently, a pipe. There was no other use of tobacco. The use of his voice, as a salesman, may also have been an etiological factor.

Laryngoscopic examination showed a low papillary growth, pink in color, with sessile base, on the upper surface of the cord at the posterior end. It was approximately 0.5 by 0.4 centimetre in diameter, and reached to the ventricle. There was no loss of motion in the cord. No enlarged cervical lymph nodes were palpable. This case seemed objectively a favorable one for laryngofissure, but from the cancer viewpoint, the long duration (ten months) and the proximity to the arytenoid and the ventricle, made it seem wiser to remove the larynx and the immediately regional lymph nodes.

The operation, October 18, 1927, consisted in the removal of the larynx, in block with the lymph-node groups over the carotid bifurcation and just below the posterior belly of the digastric, on both sides. The procedure followed the plan outlined for the two other cases, as to the larynx and the trachea. The lymph-node dissection followed the technic already referred

to, but was simpler because it was limited to the immediately regional groups. An Einhorn tube with the Rehfuß tip was introduced as in the first case reported. The post-operative course was unusually good. The wound healed *per primam*, the Einhorn tube was removed on the tenth day, and the patient left the hospital on the following day. He has had no further evidence of carcinoma. He began to use the MacKenty artificial larynx shortly after the operation and has become very proficient in its use.

DR. J. A. MACKENTY (by invitation) remarked upon the rarity with which cases of laryngeal cancer are seen in their incipiency. Last year his records showed 156 cases of cancer in and about the larynx. Most of these began as intrinsic cancer. All but thirty had become extrinsic and only three were truly incipient. Practically all the extrinsic cases were hopeless.

Primary subglottic cancer is rare and in its early stages difficult of detection. It readily escapes into the neck through the cricothyroid membrane and on this account has a much higher recurrence percentage than cancer beginning on the vocal cords.

Out of over 900 cases of laryngeal cancer seen by him in the past twenty-five years only thirty-six were women—all fairly young excepting three. Four of these were unusually young for cancer—thirty, twenty-six, twenty-four and twenty, respectively.

Since the chief warning of laryngeal cancer is in an early hoarseness and since this occurs only in intrinsic, glottic and supraglottic cancer, primary extrinsic cancer, in which the vocal cords are intact, may, and usually does, become well seated before its presence is suspected. Early cancer in this situation is painless and does not, until quite late, affect, in the slightest degree, the general well-being or the voice of the victim. His experience had led him to the conclusion that cancer is far more frequent in larynges which have been the seat of antecedent pathology: Chronic laryngitis, syphilis, rhinoscleroma, papilloma, angioma, hyperkeratosis, prolapse of the ventricle, tuberculosis, etc. In the past two years he had seen two cases of tuberculosis of the larynx, complicated by cancer, and in the far past one case presented, after removal, evidences of tuberculosis, cancer and syphilis.

In intrinsic cancer one or other cord is by far the most common site of inception and strange to say the middle third of the cord is more commonly attacked than the rest of it, due perhaps to the fact that the middle third of the cords sustain the greatest brunt of phonation. About 80 per cent. of all laryngeal cancers are intrinsic at the start and curable by the proper radical treatment.

For primary extrinsic cancer local discomfort as a diagnostic symptom takes the place of hoarseness in primary intrinsic cancer. This with a slight change in the quality of the voice makes careful investigation imperative. Pain radiating to the ear is a later sign but often present. The hypopharynx is, especially in women, the hiding place of incipient cancer. Digital examination is helpful in cancer above the larynx but he doubted its value in early cancer in the larynx. The well-developed intrinsic cancer needs

## CANCER OF THE LARYNX

nothing but the eye to label it, since in most instances its appearance is very characteristic. If any degree of success in treatment is expected the diagnosis in extrinsic cancer must be early. The lymphatics may take the disease up at once. This, however, is very variable and depends on the virulence of the disease. Some of the superlaryngeal malignancies are quite benign and slow to invade; especially is this true of cancer on the posterior surface of the epiglottis. He had had two such cases free from recurrence—one for three years and the other for eight years. In neither of these did it seem advisable to remove the glands of the neck. Many cancer patients die from the delay of too many consultations and from the allurements of radium. Unfortunately for them, many select the lethal radium route to eternity.

He believed that biopsy if not properly controlled is dangerous. What is the sense of doing biopsies on a neoplasm with cancer written all over it? In incipient conditions it may be of use. He would warn against it in tuberculosis. Many such cases are thrown over the edge by biopsy. Its findings should not weigh too strongly against negative clinical evidences. In the past ten years he had seen three positive biopsies proved to be wrong.

Laryngofissure may fit the incipient case providing St. Clair Thomson's method is used. But just when is a case incipient? After twenty-five years of inquiry he was still in doubt. Three experiences in recent years had upset his confidence in his former dogmatism. Three larynges with very incipient cancers on the middle third of one cord showed after removal (patients demanded total extirpation) on multiple section, subsurface extensions of cancer to the confines of the larynx. Here laryngofissure would have been a serious mistake. His recurrences after laryngofissure are 35 per cent., but he did not use the Thomson method in the earlier ones.

Lymphatic removal in frankly intrinsic cancer is not justifiable in view of the enormous percentage of no recurrences without it. For cancer outside the larynx it should be practically a routine procedure. Opening the lymphatic areas of the neck adds very materially to the death rate, especially if done when the larynx is removed. There is a lot to be said, however, in favor of doing everything at once and not crossing the cancer field. Several of his recurrences were not in the lymph nodes but in the flaps and some were in the skin. Lymphadenectomy would not have helped there. He had had recurrences *in loco* from six to seventeen years after laryngectomy, showing that cancer infection may remain dormant for years in the local lymphatics and break out only when these areas are subjected to strain from some other infection. He had seen melanotic sarcoma on the cervical and inguinal glands—large dark masses showing through the skin—lie dormant for five years and then overwhelm the patient in a few weeks.

The surgical mortality in his series of cases is under 3 per cent. In incipient intrinsic cancer the recurrences up to 1928 were 3 per cent. Cancer is never cured until the patient dies of some other cause. It is arrested.

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perfect satisfaction and no untoward effects. Gastroenterostomy is never indicated. Anæsthesia is a most important factor in this operation. He preferred scopolamine-morphine-novocaine anæsthesia supplemented by a minimum dose of ether *per ora*.

DR. FRANZ TOREK said that in cases of extrinsic cancer removal of the larynx is the only operation to be considered. The importance of the removal of lymph nodes involved by the carcinoma is well understood at the present time, although not many years ago this fact was not fully realized. It must not be believed that even after thorough removal of the lymph nodes one can be sure of non-recurrence in nodes, but the percentage of cures is enlarged if the removal of the lymph nodes is radical. It is a great mistake to omit taking out some of the involved lymph nodes for any reason. One cannot trust in the efficacy of X-ray help after an imperfect operation. In this field actinotherapy cannot compete with surgery, in spite of the fact that lymphocytes are strongly radiosensitive. It is a fact that many of these cases are recognized too late. In many instances it is the patient's own fault; he has become accustomed to his hoarseness. It is rather humiliating, however, that these patients should be under the treatment of laryngologists for three months or longer without the discovery of the presence of carcinoma. As to biopsy, most cases can be diagnosticated without it; but there are others in which this cannot be done. It will always be the early cases that are difficult to diagnose. If the new growth has ulcerated its characteristics are more likely to be recognized, but in an early case that has not broken down but manifests itself merely by a thickening of the vocal cords or some other portion, one should do a biopsy. In a word, biopsy will be more necessary in the early cases than in the more advanced. Among the dangers of the operation is that of aspiration of secretions. With constant aspiration of mouth secretions during the operation and by keeping the head suspended, this danger can be minimized. As general anæsthesia increases the danger of aspiration, Doctor Torek prefers the operation under local anæsthesia by anæsthetizing the third and fourth cervical nerves on both sides at the third and fourth cervical vertebræ. By doing so one anæsthetizes all the supraclavicular and cutaneous nerves. A regional infiltration in addition to that will complete the job. Such an anæsthesia usually lasts about two hours and if necessary it can be repeated. There is little pain felt by the patient. The operation has to be done with perfect hæmostasis. It is always bad surgery to work in a pool of blood but particularly so in cancer surgery, for one must be able to see everything distinctly to get around the involved area.

# BRIEF COMMUNICATIONS

## INTESTINAL OBSTRUCTION COMPLICATING ACUTE APPENDICITIS IN A CHILD OF THREE YEARS

THE following case report presents an unusual combination of features which illustrate the occasional complexity of post-operative observation and care, and the desirability of consultation in difficult cases with experimental and preclinical workers.

The patient was a child three years of age, weighing 38 pounds, who was admitted to the Evanston Hospital November 18, 1930, suffering from acute anterior poliomyelitis and presenting on admission a flaccid paralysis of the left arm and right leg. At the end of two weeks in the hospital, the child began to complain of abdominal pain which soon became localized in the appendiceal region. The abdomen was opened December 2, 1930, and an acutely inflamed appendix, plastered down by adhesions, was removed. During the process of removal the appendix ruptured and a small amount of pus escaped. The subsequent course was tempestuous; temperature  $105^{\circ}$ , pulse 140, considerable vomiting. By the fifth day, there was marked abdominal distention, projectile emesis, no flatus obtained by enema; 1,000 cubic centimetres of saline mixture were administered subcutaneously and, under nitrous oxide anaesthesia, the bowel was again opened through the left rectus muscle. A greatly distended loop of small intestine was drawn out of the wound and a Witzel enterostomy was made, using a rubber catheter for the tube. Temporary improvement followed this procedure. Frequent saline enemata were given and 10 cubic centimetres of peptonized milk were administered every hour through the enterostomy tube which was clamped for ten minutes after each injection of fluid. Meanwhile the fluid loss from the enterostomy tube was large. In an attempt to decrease this fluid loss, the enterostomy tube was clamped and opened at various intervals. Finally a cradle was placed over the child and the enterostomy tube, some 14 inches of which was outside of the body, was suspended vertically from the cradle with the distal end up and not clamped at all. In this way a vent for gas was continuously present and the weight of the column of fluid in the tube prevented undue fluid loss.

December 10, eight days later, a whole-blood transfusion of 250 cubic centimetres was given, the cannula was left tied in the patient's vein so that every ten minutes 5 cubic centimetres of dextrose-Ringer's solution might be allowed to flow into the vein. Moderate reaction to the blood transfusion occurred; pulse 146, temperature  $104.8^{\circ}$ ; repeated gastric lavage. The fluid intake was as follows: oral, 190 cubic centimetres; through enterostomy tube, 476 cubic centimetres; intravenous, 965 cubic centimetres; total, 1,631 cubic centimetres. The output was: urine, 330 cubic centimetres; drainage from enterostomy tube, 690 cubic centimetres; total, 1,020 cubic centimetres.

At this point, because of the involved physiological considerations, Dr. A. C. Ivy, Professor of Physiology at Northwestern University Medical School, was called into consultation. Doctor Ivy proposed the employment of a food for intestinal feeding which had been evolved in his department by Dr. H. G. Scott and which had been used successfully in animals.\* The formula, permission to publish which has been courteously accorded by Doctors Ivy and Scott, is as follows: Milk, 3 quarts; water, 3 quarts; dried peptone (Merck), 100 grams; cane sugar, 150 grams; wheat flour, 300 grams. In the

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\* Full details concerning the experimental consideration by which this formula was obtained will shortly be published by Professor A. C. Ivy and Dr. H. G. Scott in a separate communication.

preparation of the food, to the water add the sugar and heat to 130° F. and add the peptone; heat for four minutes, then add this solution gradually to the flour, making a paste, then add all the milk. The mixture is then brought to 212° F. and heated at the sub-boiling temperature for three minutes, or longer, until the solution is about as thick as cream soup. One hundred cubic centimetres of this food were administered by the enterostomy tube every two hours, taking care to drain the tube first. After twenty-four hours, 5 grams of sodium chloride were added to each quart of the food. The quantity was reduced to 50 cubic centimetres every two hours. On this day also, the appendectomy incision was explored laterally by finger and an abscess cavity opened up from which 2 ounces of pus escaped. A counter incision was made through the right flank into this cavity and drains were inserted.

On the following day, it being evident that the bowel was not tolerating well the quantities of fluid which were injected into it, and the child being able but poorly to swallow fluids that were administered orally, a nasal feeding tube was passed through the nose into the stomach and 50 cubic centimetres of the "food" were injected through this tube into the stomach. Every two hours thereafter, this procedure was repeated, alternating with 25 cubic centimetres of the "food" every two hours by the enterostomy tube. Gradual increase in the amount of food administered by the nasal tube marked the next two days. The nasal tube was aspirated before each injection to ascertain the presence or absence of fluid in the stomach. The child improved rapidly and on December 16, 1930, there was a liquid defecation. On the 18th and 19th there were several small stools, but on the 20th, symptoms of obstruction again developed. It seemed probable that an acute strangulation of the bowel was taking place so that on December 22, under avertin and ether anaesthesia, the abdomen was again opened through a left paramedian incision after observing great care in the skin preparation. A loop of the small bowel was found densely adherent to the anterior abdominal wall in the region of the original right paramedian incision. This adhesion had caused an acute angulation of the bowel which almost obliterated its lumen. The bowel was freed from this attachment and dropped back into the abdomen. The wound was closed; hypodermoclysis of normal saline given. The patient withstood this very well and from then on convalescence was uneventful. The enterostomy tube was removed on December 23, bowel movements began on the same day and have continued regularly since. As the patient's strength improved, the nasal feedings were gradually decreased and oral feedings were increased. There had been a definite regression of the paralysis of the left arm. December 31, a small abscess which had developed in the final incision was drained. January 7, 1931, all wounds were healed, the child was happy and normal in appearance, and was discharged from the hospital.

FREDERICK CHRISTOPHER, M.D.,  
*of Winnetka, Ill.,*  
*Surgeon: Evanston Hospital.*

### "ANCHORING" RADON SEEDS AT BASE OF TONGUE

IN A paper published five years ago (ANNALS OF SURGERY, vol. lxxxiii, p. 598, May, 1926) I first advocated the use of removable platinum radon seeds in the treatment of malignancy of the tongue. I stated that I had found this new applicator capable of "complete intra-neoplastic insertion, so that there is no chance of dislocation nor expulsion," and that the fact that the seed is completely buried in the malignant tissue gave it a great advantage over the platinum needle "as regards retention of position and non-interference with function of the surrounding parts." After using the

## ANCHORING RADON SEEDS IN TONGUE

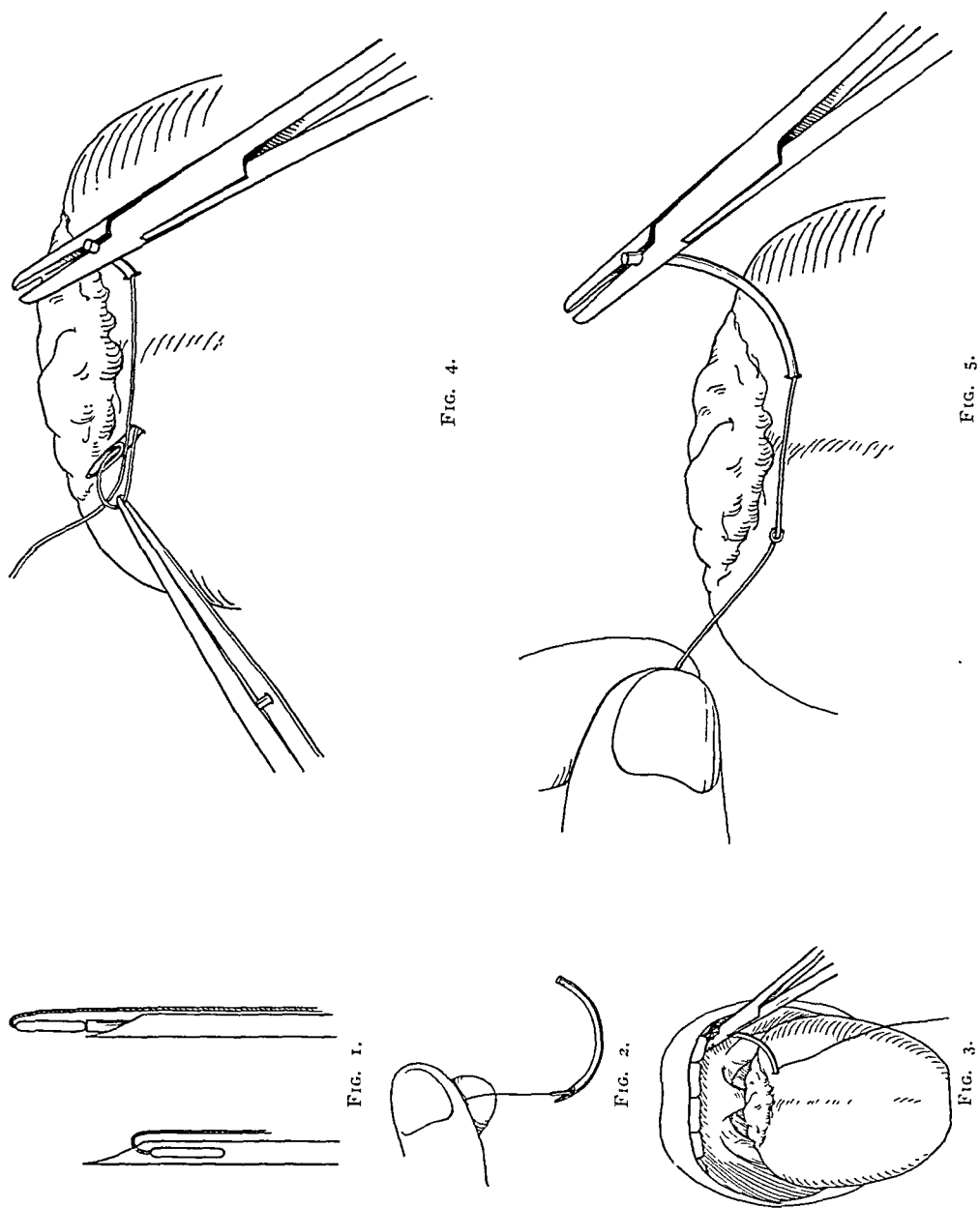
method very extensively for more than five years I now find that while my first experience has remained uncontradicted in most cases, situations occasionally arise when my original position must be somewhat modified. Deeply implanted seeds regularly remain in position for as long a time as we desire to keep them there. Now and then those placed near the surface show a tendency to become dislodged by the continuous mobility of the parts involved. Though such a situation was decidedly rare, its very frequency made it particularly distressing when it did occur.

I have now devised a plan of "anchoring" superficially placed seeds which will, I trust, do away with any possibility of their being accidentally dislodged. The device which I am about to describe is the outcome of practical experience, and the chastening influence of a few failures and disappointments. It is particularly designed for such situations as the pharynx, hitherto regarded by many radium therapists as a place where implantation was impractical and for the tongue or other parts where mobility is so great as to interfere seriously with the retention of such foreign bodies as metal radon seeds.

The danger commonly apprehended by those unfamiliar with radium technic is that the seeds will "fall out." This does, of course, occasionally happen. A far more frequent situation, however, is the migration of the seeds from their original positions so that the radiation they give off is not properly distributed. In one case of which I have knowledge wherein permanent implantation was employed, all the seeds distributed through a lesion at the base of the tongue worked their way through the tissues until they were concentrated at one spot. This made the radiation at that point so intense that necrosis was inevitable and the entire tongue eventually sloughed off as a result. This was, no doubt, an extreme case, yet the dangers which it illustrates are always present when seeds are permanently implanted in areas where considerable mobility is inevitable. "Anchoring" seeds in such a situation is a safeguard imperatively demanded.

To carry out the new technic which I have mentioned, it has been necessary to convert the loading-slot implanter—which bears a certain resemblance to a breech-loading firearm—into a "muzzle loader." The seeds which were formerly placed in the loading-slot and pushed down the barrel of the instrument by the insertion of the obturator are now inserted into the point of the implanter as shown in Fig. 1.

In Fig. 2 is shown a curved implanter with the seeds inserted as in Fig. 1. Fig. 3 indicates how the needle-like implanter with the point carrying the thread (inserted point first and thread-end protruding) is thrust into the tissues at the base of the tongue. The point emerging, as shown in Fig. 4, the thread forms a loop about it which may be caught by a second pair of forceps and drawn out as shown in Fig. 5. In Fig. 6 the loop is pictured drawn down to make a knot, the final position of which in relation to the seed is illustrated in Fig. 7.



FIGS. 1 to 9.—Showing steps in anchoring radon seeds in a tongue.

# ANCHORING RADON SEEDS IN TONGUE

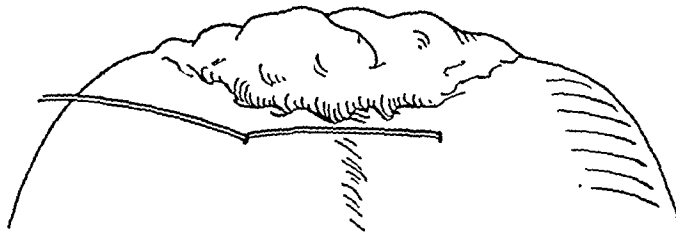


FIG. 6.

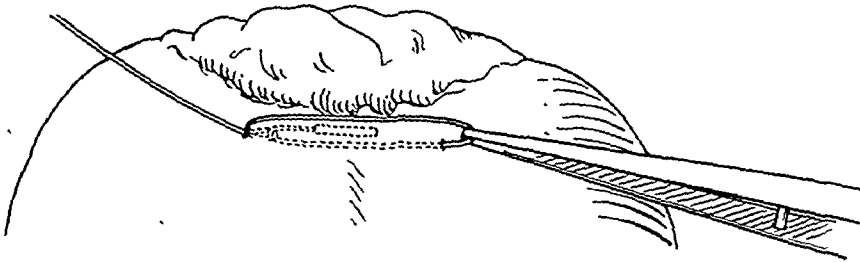


FIG. 7.

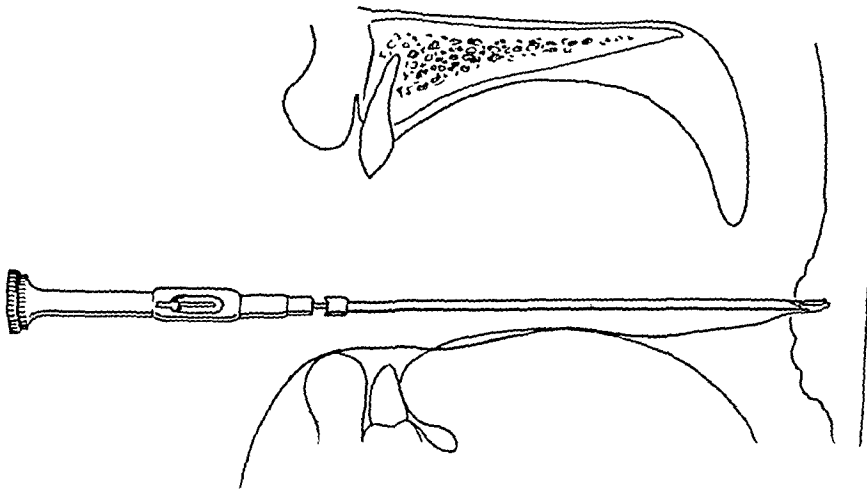


FIG. 8.

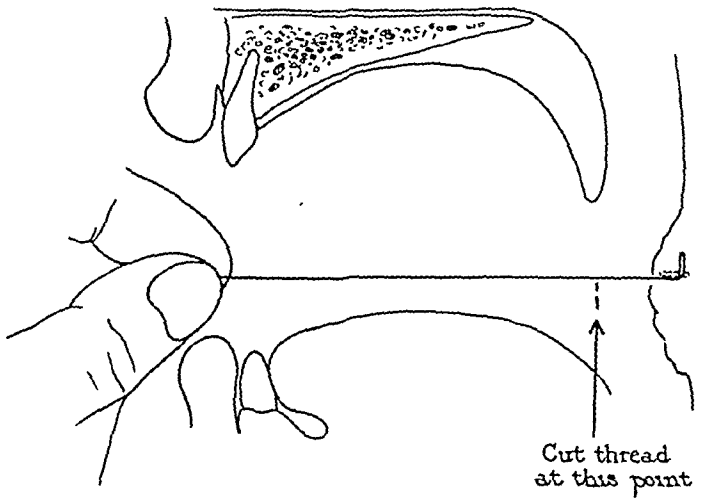


FIG. 9.

In Figs. 8 and 9 is shown a method of "anchoring" the seed in the wall of the pharynx, which has already been mentioned as an exceptionally difficult situation in which to insure even distribution of the radioactive centres for the length of time necessary to give adequate dosage. The seed is placed in the point of the implanter with the thread-end protruding. When the implanter is thrust into the tissue the thread precedes the seed as shown in Fig. 8. The instrument being withdrawn, gentle traction is exerted upon the thread, so that the angle at which the seed lies is changed. Its position is now perpendicular instead of horizontal. Traction also causes the thread to loop about the end of the seed, making it much more difficult to dislodge than would otherwise be the case. The thread is then cut off as close to the pharyngeal wall as possible, only enough thread being left to permit forceps to take hold for later removal of the seed.

The implantation of lesions of the mouth and throat will be found greatly facilitated by the employment of these simple safeguards. The assurance that the seeds will neither fall out nor migrate from the position in which they were originally placed permits the physician to proceed with more confidence, while the actual advantages of proper distribution in all situations are so great as to enhance the value of the treatment to a very appreciable extent.

JOSEPH MUIR, M.D.,  
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## NECROSIS OF URETER

### FOLLOWING REPEATED INJECTIONS OF MERCUROCHROME AND SILVER NITRATE SOLUTIONS

FORTUNATELY, destruction of the ureter by chemical injections in the course of diagnosis or treatment is rare, so far as we have any published reports. Such reports as I have seen are those of the accidental introduction of caustic chemicals in an effort to make diagnostic ureteropyelograms. This occasional catastrophe has resulted in many clinics refusing to allow bilateral injections for pyelograms at one sitting. In none of these reported cases have I seen any ureterograms taken after the destructive injection, so that the X-ray appearance of the ureter ulcerated as a result of destructive chemical injections is not a matter of record. I have seen no picture of it, that we may compare its destructive lesion with the ureter ulcerated as a result of infection, such as tuberculosis. It is to fill this vacancy in our album of ureterogram pathology that I wish to place on record the following case of the ureter ulcerated by injected chemicals.

Mr. X., a young man, was taken sick with dysuria and frequency and was sent to the local hospital for urological examination by the attending urologist. He was running the temperature of acute pyelitis, and the report after cystoscopy was pyelitis with cystitis. A bilateral ureteropyelogram was taken. (See Fig. 1.) Although the picture is poor it is good enough to demonstrate the normally smooth right ureteral wall. The

# CHEMICAL DESTRUCTION OF URETER



Fig. 1.—Ureterogram on admission to hospital. Note smooth, normal margin.



Fig. 2.—Ureteropyelogram made eight weeks after Fig. 1 was made. Note the dilated, ragged, irregular outline.



Fig. 3.—Tube in kidney following pyelotomy. Note sodium iodide can not be made to go down into.



right kidney was sterile and functioning normally. The treatment consisted in forced fluids and rest. His temperature was normal in five days and the patient went home. The condition promptly recurred and he returned to the hospital, where he was re-cystoscoped and catheters left up both ureters. On this examination the laboratory reported pus from both kidneys. No pyelograms were taken and the catheters were left in position in the ureters for fifteen days. Each day the catheters were washed out with sterile water and there were injected into them 2 cubic centimetres of 1 per cent. mercurochrome and 3 cubic centimetres of 1 to 2 per cent., silver nitrate.

At no time during these injections did the patient complain of any unusual right-sided pain. In fact, the bedside notes refer to left renal pain.

The patient's condition did not improve. After he had been ill about eight weeks he came to the Hartford Hospital under my care in an extremely serious condition. At this time the symptoms were severe pain in the right kidney and dysuria, his temperature varying from 102° to 105°. I then cystoscoped him and got a double ureteropyelogram, as seen in Fig. 2.

He was so ill that I felt he would not stand a nephrectomy, so I did a nephrotomy under local anæsthesia and placed a tube into the kidney pelvis, as shown in Fig. 3. No effort was made to explore the ulcerated right ureter. We subsequently made many examinations for tubercle bacilli, with negative findings. X-rays of the chest revealed no sign of tuberculosis. Yet because of the ragged appearance of the right ureter, I made a diagnosis of probable tuberculosis.

After about two months' draining through the pyelotomy wound, the patient recovered enough for a nephro-ureterectomy. My diagnosis was still probable tuberculosis. I promised this boy's friends to take out his kidney and attempt to remove his large ulcerated old ureter. Imagine my surprise at not finding this ureter when I looked for it. I decided to free the kidney up first and in that way locate the ureter. The kidney was easily freed up in spite of the old adhesions. I severed the vascular pedicle and lifted this kidney right out of the wound. There was no ureter below the pelvis. My dissection was very clean, even down to below the iliac vessels, but nowhere was there any trace of the ureter left. The wound was drained. Following this operation the patient made an uneventful recovery.

When I realized that I had been dealing with a pathological condition following the injection of chemicals in the ureter, I reëxamined the old bedside notes, and there is no record of the injection into these kidneys of anything but 12 per cent. sodium iodide for the first pyeloureterogram and later, during the fifteen days that the catheters lay in the ureter, the injection of the 2 cubic centimetres of 1 per cent. mercurochrome and 3 cubic centimetres of 1 to 2 per cent. silver nitrate.

It is difficult to speculate as to just what chemical destroyed this ureter and why the destruction was unilateral, when catheters were presumably up each ureter. One is forced to choose from the following possibilities: Either the catheter slipped out of the left ureter without this fact being recognized and some unrecorded corrosive was accidentally injected; or else different chemicals were injected into the two catheters, that to the right being accidentally strong, which was unlikely; or else there was some mechanical condition in the right side which prevented the outflow of the mercurochrome and silver nitrate after it was injected, so that these small amounts, at the dilution used, were sufficient, when repeated daily over fifteen days, to cause destruction of the ureter.

## MIKULICZ OPERATION CLAMP

So far as the actual evidence at hand is concerned the last supposition seems most probable.

Therefore, it is especially important that the possibility of such a disaster must be kept in mind by all surgeons who are injecting repeated doses of 1 per cent. mercurochrome or 1 to 2 per cent. silver nitrate, or the combination of the two, especially where these corrosives may return down the ureter around the catheter and be retained in the ureter by a tight sphincter. It is well known that 1 per cent. mercurochrome when it leaks around a vein after intravenous injection, becomes destructive in its effect on the tissues.

### CONCLUSIONS

1. A ureterogram showing a destructive ureteritis the result of the injection of corrosive chemicals is here presented.
2. The similarity of this picture to tuberculous ureteritis is noted.
3. It would seem that the repeated injections of 2 cubic centimetres of 1 per cent. mercurochrome and 3 cubic centimetres of 1 to 2 per cent. silver nitrate into retained ureteral catheters, if done as often as once a day for fifteen days in succession, has the potentiality of destroying the ureter under conditions, as yet unknown, but very possibly when the return flow is poor because of some ureteral spasm.

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## MIKULICZ OPERATION CLAMP

IN THE Mikulicz stage operation for tumors of the sigmoid flexure of the colon, the clamps generally used to cut through the double-barrel spur of the bowel are awkward and cumbersome with the long handles protruding



FIG. 1.—Mikulicz operation clamp to crush through the contact areas after double-barrel spurs in cases of tumor of the sigmoid flexure of the colon.

far above the dressings. The clamp worries the patient and requires careful handling to avoid pulling or tearing out of the bowel.

The instrument herein illustrated and described avoids all the disadvantages of such a clamp and functions very well in making the opening between the two loops of colon long enough and sufficiently wide for good function

and a successful anastomosis. It may be used after removing the exposed tumor by the old method or following the use of the Fred Rankin crusher.

The instrument is  $5\frac{1}{4}$  inches long. The crushing blade is  $3\frac{1}{2}$  inches from the centre of the screw in the joint. The width of the crushing blade is seven-sixteenths of an inch. The open portion of the blade is four-

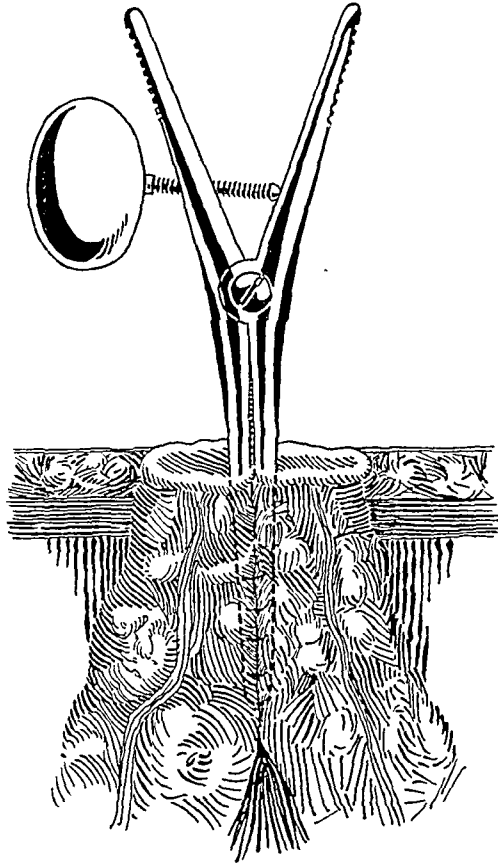


FIG. 2.—Shows the clamp in position.

sixteenths of an inch across and  $2\frac{3}{4}$  inches long. The teeth intermesh so there is no danger of the instrument's slipping, once it is set and screwed tight. When the blades are in position for crushing, the set screw is tightened and the crusher thus held firm. The dressings are placed around the handles.

CARL R. STEINKE, M.D.  
*Akron, Ohio.*

### DISPOSITION OF THE HEAD OF THE FIBULA IN HIGH AMPUTATIONS OF THE LEG

THE part of fibula left in a stump not connected with the tibia and under little or no muscular control frequently becomes a menace. It does not synchronize with the movements of the tibia when an artificial limb is being worn. Consequently there is a disturbance of the tissues between the bones. In some cases this disturbance causes pain. In other cases it induces a

thickening of the tissues and in other cases it induces a tumor, which takes on growth continually and finally forces the bones apart. An artificial leg fitted perfectly when delivered will be a painful thing to the wearer when the fibula is forced so far away from the tibia that it brings pressure on the walls of the socket.

The artificial limb maker, of course, is called upon to remove material to accommodate the fibula and relief is obtained. But in a very short time the fibula, having continued in its travel, reaches the wall of the socket under pressure and removal of further material is necessary. This continues until the socket is completely cut away and a new one is necessary, or the wearer is obliged to buy a new leg complete, but in many cases it has induced the wearer to abandon the use of an artificial leg.

The fibula is the most sensitive bone in the entire leg. No part of it will endure pressure for any length of time. This is a bone that is not necessary to control a limb. The tibia is equal to meet all demands. Why then let the remains of the fibula remain in the leg?

GEORGE E. MARKS,  
*New York City.*

## BOOK REVIEWS

ABDOMINO-PELVIC DIAGNOSIS IN WOMEN. BY ARTHUR JOHN WALSCHIED, M.D. 8 vo.; cloth; pp. 1000; C. V. Mosby Company, St. Louis, 1931.

Too many of our recent books on Gynæcology have been practically merely illustrated works for quick reference showing an operation fitted to a particular condition, and tending to carelessness on the part of the great majority of men. This is an excellent book to be used as a reference work for those who wish to improve their diagnostic ability and technic, and is devoted in its entirety to that purpose. The introductory chapter includes a study of posture and poise, which elements are generally recognized as having an immense influence on the possibilities of the development of characteristic gynæcological conditions. The chapter on etiologic factors is complete and very helpful. This is followed naturally by the symptomology which would accrue from a knowledge of the first two chapters. It is noted that no mention of *trichomonas vaginalis* as a cause of vaginitis is made. This is the only serious criticism of the volume.

The special chapters on the diseases of the various organs are not verbose but contain all the salient points necessary for a complete study of an individual case. The author has been very liberal in giving credit to his references and has produced an index in keeping with the remainder of his work. One will learn from this book not so much how to operate but rather when to operate, and it should be considered as a companion work to all books of operative gynæcological technic.

ALBERT M. JUDD.

COLLECTED PAPERS FROM THE SECOND SURGICAL DIVISION OF THE NEW YORK HOSPITAL. By THE SURGICAL STAFF, 1930.

The last collection of papers by the staff of this division was effected in 1923 and consisted chiefly of follow-up studies or late results. The present volume contains some twenty-eight articles dealing largely with the same phase of surgical research, in the preparation of which seven members of the staff have participated.

The volume is well bound in cloth and contains 276 pages with numerous illustrations, the publishers' reprints of the various articles having been used in its construction. They lend themselves fairly well to this procedure. This effort of the Second Division of the New York Hospital is to be highly commended in that it not only indicates the literary activities of the members of the staff but adds impetus to the preparation of future studies when the author appreciates that in such a volume his efforts will receive further consideration.

JAMES T. PILCHER.

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**ANNALS OF SURGERY**

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## THE SURGICAL TREATMENT OF BLEPHAROSPASM\*

BY CHARLES H. FRAZIER, M.D.

OF PHILADELPHIA, PA.

FROM THE NEUROSURGICAL CLINIC OF THE UNIVERSITY HOSPITAL

BLEPHAROSPASM, though a lesion of seemingly minor significance, assumes a major rôle in the mind of the patient. Blepharospasm, or facial tic, as other spasmodic conditions, including spasmodic torticollis, is of unknown origin. There may be more than one etiologic factor, but it is difficult in the individual case to ascribe the cause.

Blepharospasm is more than an annoyance. The sensitive woman may cut herself off from all social contacts. The business man considers himself handicapped. If both eyes are involved, driving an automobile is out of the question, crossing highways is dangerous. In reading or writing there are disturbing interruptions when the spasm closes both eyes.

Until Dr. H. W. Williams (Journal of the A. M. A., December 29, 1928, vol. xci, No. 26, p. 2053) suggested denervation of the individual muscles involved, the treatment of blepharospasm by any means was unsatisfactory. In 1901, Kennedy proposed anastomosis of the facial to the spinal accessory nerve. In 1906, Speville (Clin. Ophth., vol. xii, p. 131, Paris, 1906) was the first to advise the injection of alcohol. We all know from experience what a dismal failure this was. Later, he proposed stretching the nerve. Coppez, in 1921, and Sachs, in 1925, proposed two rather complicated plastic operations, one on the orbicularis oculi, the other on the upper lid. Finally, in December, 1928, Dr. H. W. Williams proposed the operation which in principle we are about to describe.

It is my purpose in this contribution merely to record a technic which has served me in good stead in four operations. From an inspection of a number of specimens, from a review of my operative notes, and from an inspection of the illustrations in anatomic charts, I at once realized there is a great variation in the exact number of nerve filaments as they present themselves in the field of operation. And be it remembered that the filaments to be isolated for section are in diameter not larger than strands of fine silk or hair filaments. The dissection therefore is tedious. Furthermore, a single filament at the level exposed on stimulation might supply more than one muscle. For example, in one case, stimulation of one filament caused contraction of both orbicularis palpebrarum and occipitofrontalis; of another, contraction of both orbicularis palpebrarum and the muscles at the angle of the mouth, so that while the nerves must be first exposed by dissection, the number to be cut must be determined with the aid of electric stimulation. Before discussing the technic, I submit the notes of four operations.

\* Read before the Philadelphia Academy of Surgery, February 2, 1931.

CASE I.—Mrs. V. H., aged thirty-eight, file No. 18537. Facial spasm, left. Duration, nine years. *Operation*.—April 9, 1930. A curved incision was made with the convexity forwards, two-thirds above and one-third below the anterior portion of the zygoma. Thus the anterior and superior margins of the parotid gland were exposed. By blunt dissection, three nerve filaments were exposed. Stimulation of the upper of the three caused contraction of the corrugator supercili and orbicularis palpebrarum. Stimulation of the middle filament caused contraction of the orbicularis palpebrarum. The third filament was much smaller; stimulation caused contraction of the orbicularis

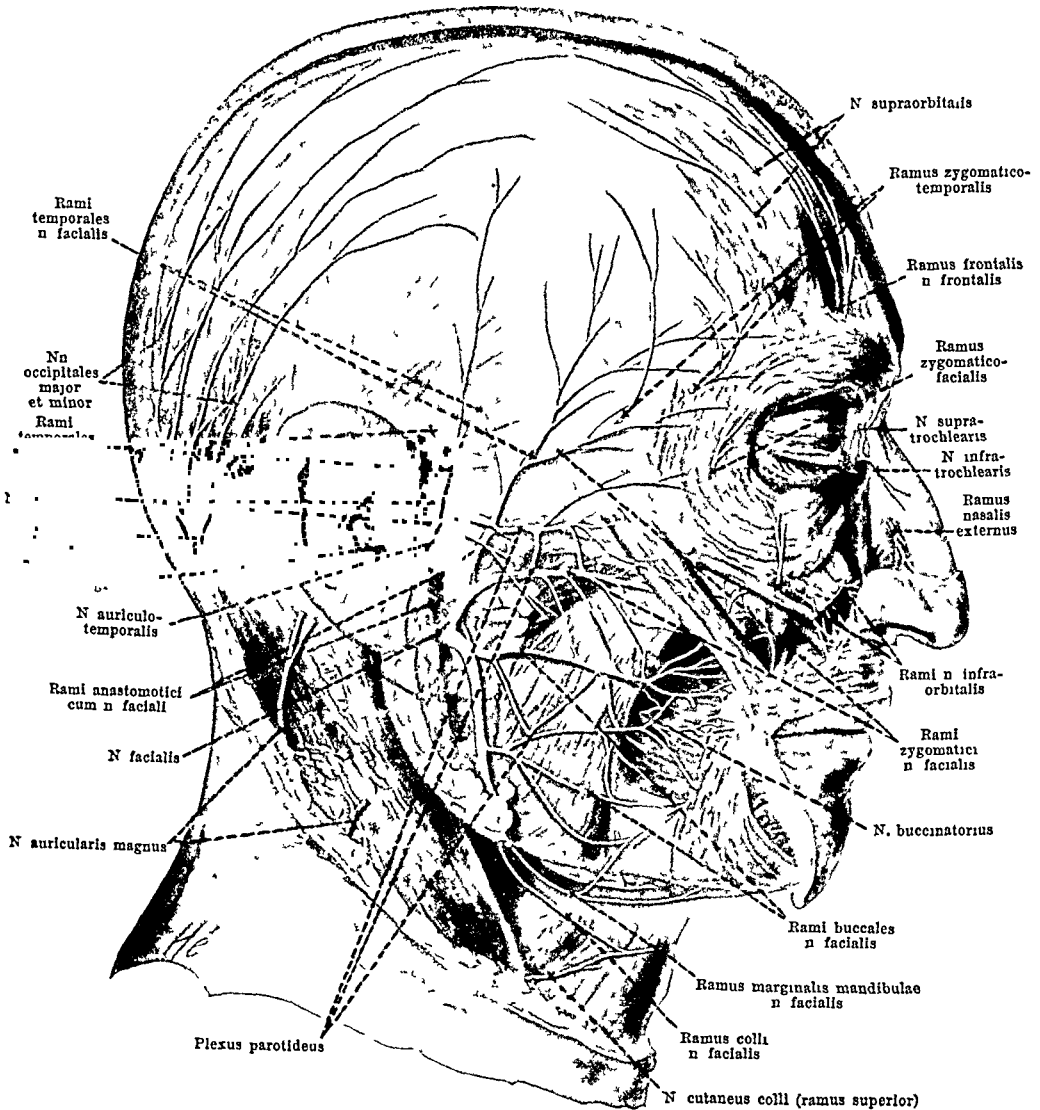


FIG 1.—Facial nerve and its distribution (From Spalteholz)

palpebrarum and elevation of the angle of the mouth. The two upper branches were cut and the third crushed with a hæmostat. The patient was then tested to make sure that this nerve could be sacrificed without causing any drooping at the angle of the mouth. She could elevate the angle of the mouth freely but on showing the teeth there was a slight droop. This was so trivial that we felt justified in cutting the third filament. At the conclusion of the operation the spasm was entirely relieved and could not be induced as it could before by the patient's closing the eye forcefully.

CASE II.—Mr. E. M., aged fifty-six, file No. 19985. *Diagnosis*.—Blepharospasm of

both eyes. Duration, two years. *Operation*.—October 21, 1930. A rectangular incision with the horizontal limb over the zygoma with a vertical extension from its anterior extremity. A triangular flap was reflected backwards and by blunt dissection the following nerves were exposed: (1) The buccal branch, much larger than the rest, the chief supply of the lower facial distribution. (2) The next filament above caused contraction of the orbicularis palpebrarum only. (3) Next above, a filament which on stimulation caused contraction of both the orbicularis palpebrarum and corrugator supercilii. (4) A filament which on stimulation caused contraction of the corrugator supercilii and occipitofrontalis.

One by one these three branches were cut and the patient could still close the eye, though feebly. Searching for a remaining supply to the orbicularis palpebrarum we found a filament given off from the buccal branch, which on stimulation contracted this muscle. When this was severed, the orbicularis palpebrarum was impotent.

CASE III.—E. M., aged fifty-six, file No. 20983. *Diagnosis*.—Blepharospasm, left. Duration, two and one-half years. *Operation*.—January 27, 1931. A rectangular incision was made under local anæsthesia, in accordance with our previous directions. With some difficulty the superior and anterior margins of the parotid gland were isolated, and in this case the gland extended well up above the upper margin of the zygoma. We then proceeded by blunt dissection to isolate the nerves as they appeared at the edge of the parotid gland. In this particular case six or seven filaments were uncovered, with the following results (Fig. 2):

- (1) Stimulation of No. 1 caused contraction of corrugator supercilii.
- (2) Stimulation of No. 2 caused contraction of corrugator supercilii.
- (3) Stimulation of No. 3 caused contraction of corrugator supercilii and orbicularis palpebrarum.
- (4) Stimulation of No. 4 caused contraction of occipitofrontalis.
- (5) Stimulation of No. 5 caused contraction of occipitofrontalis and corrugator supercilii.
- (6) Stimulation of No. 6 caused contraction of levator augularis.
- (7) Stimulation of No. 7 caused contraction of orbicularis palpebrarum.

Curiously enough, at no time during the operation did we get a vigorous contraction of the orbicularis palpebrarum. I attribute this to the fact that this operation was done under local anæsthesia, and the novocaine must have deadened the sensitivity of the nerve.

The dissection was continued down the anterior margin of the parotid gland until the buccal branch was uncovered. As the patient could still close the eye, we looked for a branch from this to the orbicularis palpebrarum which we have found in another case, although stimulation of this did not cause any contraction again probably because of novocaine inhibition. This small twig was cut.

After all the above filaments were cut, the patient could still close the eye, but not vigorously. He could elevate the angle of his mouth but he could not elevate his brow. In other words, we did not have a complete paralysis, although, so far as we could see, there was not the vestige of a nerve filament left which made its emergence from the superior margin of the parotid gland, around to the buccal division.

The wound healed by first intention and when discharged from the hospital five days after operation, there had been no spasmodic movements.

CASE IV.—Mrs. T. E. B., female, aged forty-one, file No. 20572. *Diagnosis*.—Blepharospasm, right. Duration, eight years. *Operation*.—December 2, 1930. Under local anæsthesia, a rectangular incision was made and a triangular flap reflected. The margins of the parotid gland were exposed and little by little, by blunt dissection, several filaments were exposed, along the superior margin and 2 centimetres down the anterior margin of the parotid gland. The last two filaments, when stimulated and before section, caused not only contraction of the orbicularis palpebrarum but violent movements at the angle of the mouth.

The anatomic picture and the distribution and size of the branches were entirely different from anything we have seen in our other operative experiences. When we had



finished the operation the patient could still close the eye although the spasmodic contractions had been arrested. The wound healed by first intention, and when the patient was last heard from three months after the operation there had been no return of spasm.

*Discussion.*—From these operative experiences, it will be seen at once how the number of branches to be cut may vary. The incision should be planned to expose both the anterior and the superior borders of the parotid gland. One limb of the rectangular incision must parallel the zygoma at its inferior margin; the other, at right angles, extends downwards from the anterior limit of the horizontal limb. Thus a triangular flap is reflected which exposes the desired field. Variations will be found in the boundaries of the

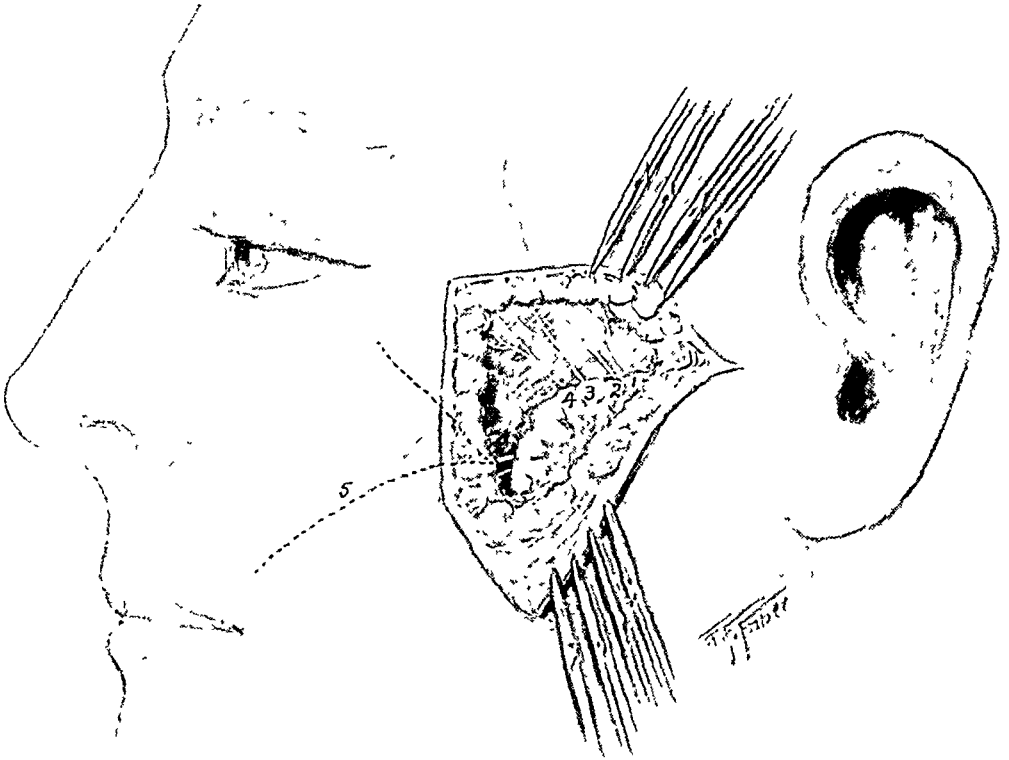


FIG. 2.—This drawing must be accepted as a rather rough sketch of about what one may see in an operation for exposure of the upper division of the facial nerve. It must be remembered that in our series no two cases were exactly alike. There was the widest variation in the number, size and distribution of the several branches. (1)—Branch to the corrugator supercilii. (2)—Branch to occipitofrontalis and corrugator supercilii. (3)—Branch to occipitofrontalis. (4)—Branch to corrugator supercilii and orbicularis palpebrarum. (5)—Buccal branch supplying the levator angularis with a small branch distally supplying the orbicularis palpebrarum.

parotid gland. Sometimes the gland spreads out over the zygoma. It is not always easy to identify the margins of the gland. The nerves we seek lie between the superficial fascia and sheaths of the underlying muscles. So small are the nerve filaments that they can be exposed only by gentle and blunt dissection. Since one can identify the individual nerve filaments only by stimulation it is better not to use a local anæsthetic as this may negative the response of the nerve to stimulation. At least, in one of the series, the only one in which a local anæsthetic was used, the responses were not so active as they were in the other cases. The initial incision may be made under

## SURGERY OF BLEPHAROSPASM

nitrous-oxide anæsthesia. To secure permanent results, the nerve should be cut and not, as has been suggested, injected with alcohol.

While the condition which the operation has been designed to relieve is commonly spoken of as blepharospasm, muscles other than the orbicularis palpebrarum play a part and it is not always easy to analyze the movements. In one of our series the spasm of the corrugator supercilii seemed more vigorous than that of the orbicularis palpebrarum. These movements were wholly involuntary and uncontrollable. But superimposed upon this there was an equally vigorous contraction of the occipitofrontalis, which appeared

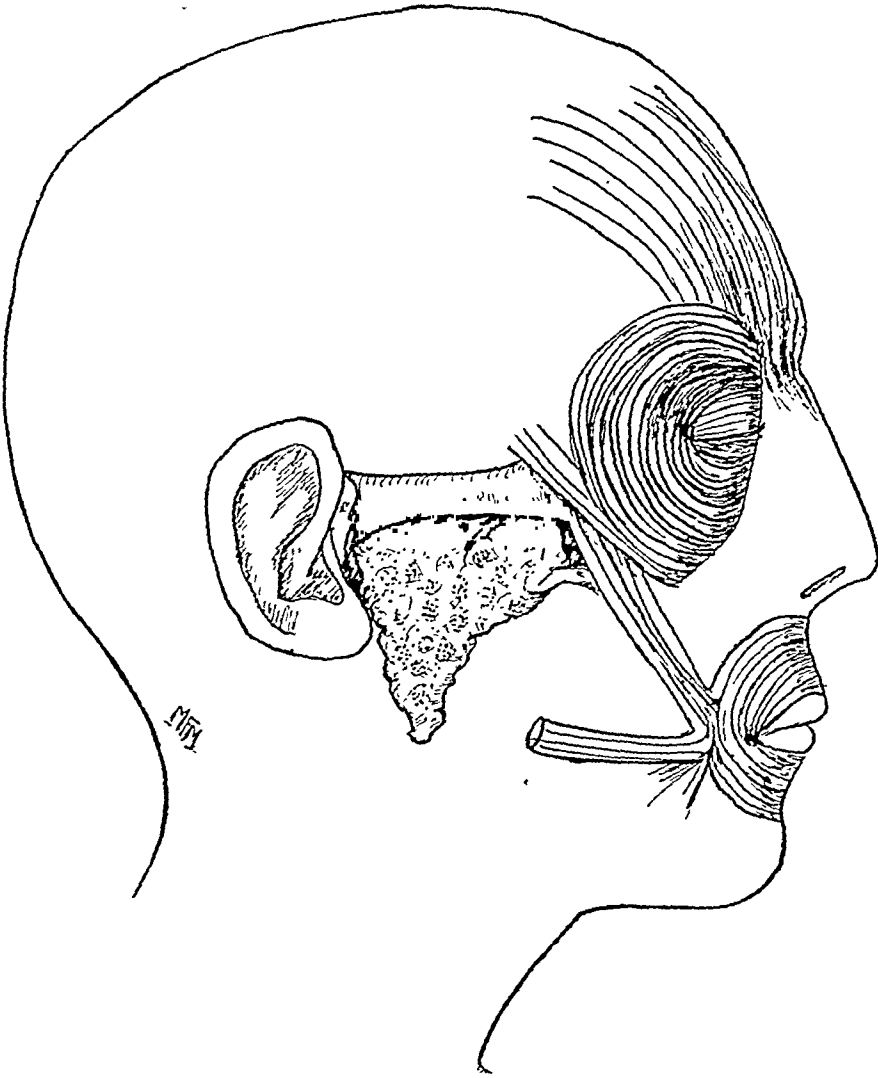


FIG. 3.—Anatomic sketch to show relationship of the important structures concerned and the important muscles involved in blepharospasm, together with the important anatomic landmarks involved in the operation.

to be a voluntary effort on the part of the patient to raise the upper lid and open the eye.

In one of the series the blepharospasm was only part of a tic in the whole facial distribution. But the spasmodic movements seemed to begin about the eye and spread to the region of the mouth. And when, by operation, the blepharospasm was arrested, the overflow to the angle of the mouth disappeared.

Sufficient time has not elapsed to speak of permanent results. Thus far, the immediate post-operative results have been eminently satisfactory.

# TREATMENT OF PULMONARY ABSCESS BY BRONCHOSCOPY\*

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THE treatment of pulmonary abscess, contrary to general impression, constitutes one of the most difficult of therapeutic problems. It is not amiss to call attention to the high mortality in such cases. It has been estimated that in approximately 50 to 70 per cent. of cases of pulmonary abscess in which treatment is not given, the termination is fatal. Lord, in a careful study of pulmonary abscess, estimated that healing is spontaneous in 10 per cent. of the cases. Graham, however, placed the percentage at more than 25. It is well known that absolute rest, postural drainage and supportive measures will lead to recovery. However, there remains a large group of cases in which further treatment is necessary. In the past, operative procedures have been the choice. Unfortunately, the mortality rate from surgical interference has been extremely high, with the uncertainty of obtaining absolute cure. Muller, from a review of the literature of pulmonary operations for abscess, estimated the mortality rate at approximately 35 per cent.

In recent years, bronchoscopy has come to be a valuable aid in the treatment of pulmonary abscess. Yankhauer, in 1916, first called attention to the possible value of bronchoscopy in the treatment of pulmonary suppuration, especially pulmonary abscess. His work was soon followed by that of Lynah, who contributed further evidence of its value. Since then, rapid strides have been made in the treatment of pulmonary abscess by bronchoscopy, and it is now regarded as one of the most valuable methods of treatment.

Before considering the results obtainable through bronchoscopic drainage of pulmonary abscess, the importance of accurate diagnosis should be emphasized. Tuberculosis, bronchiectasis, empyema, foreign body, and tumor of the bronchus, both benign and malignant, may produce symptoms closely simulating pulmonary abscess. Such diseases must be accurately distinguished from pulmonary abscess as they may constitute entirely different therapeutic problems. It is, furthermore, necessary to remember that any one of the foregoing diseases may be associated with pulmonary abscess and consequently influence treatment. It is well to emphasize that bronchoscopy is not only a valuable therapeutic agent but a necessary procedure in the accurate diagnosis of pulmonary abscess in association with röntgenograms, history taking and the general examination. In spite of the greatest care, it is not always possible absolutely to differentiate the foregoing diseases.

In the last five years, 140 patients with pulmonary abscess have been

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\* Submitted for publication March 30, 1931.

## BRONCHOSCOPY FOR PULMONARY ABSCESS

observed at The Mayo Clinic, of whom 105 were treated bronchoscopically. This report concerns those cases. Seventy-six of the patients were males and

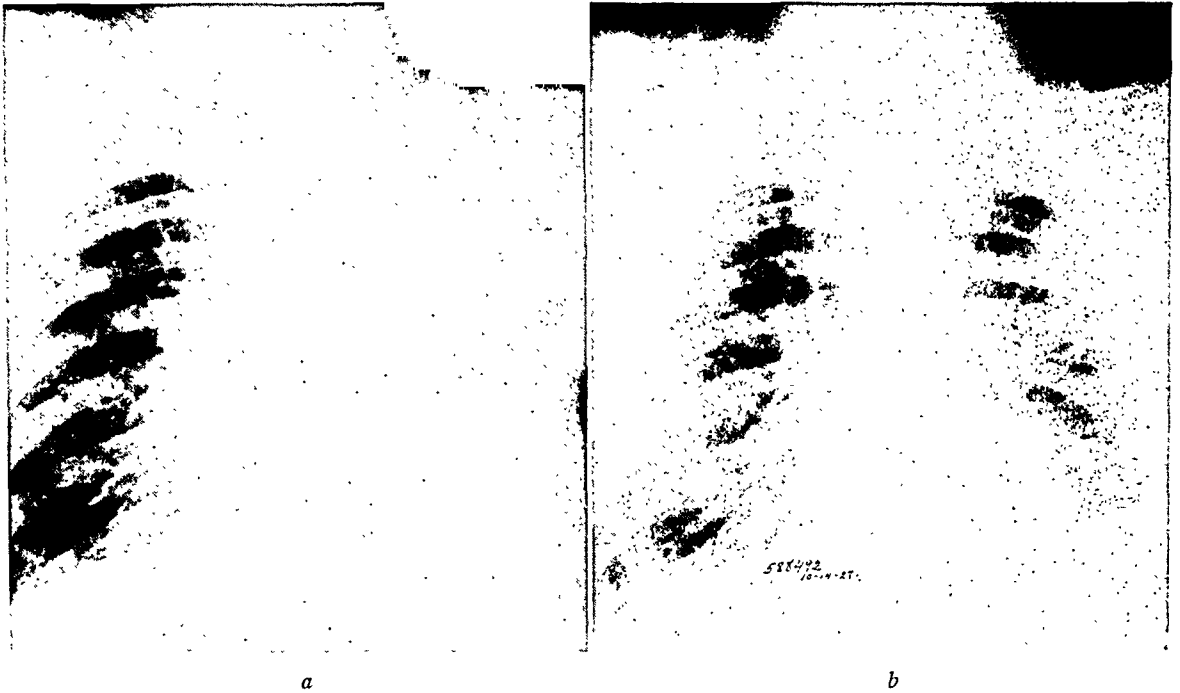


FIG. 1.—*a*, Post-pneumonic pulmonary abscess of ten months' duration; *b*, improvement after three bronchoscopic aspirations.

twenty-nine were females. The age incidence is rather striking. Although the condition may occur at any age, it is by far more common in the prime

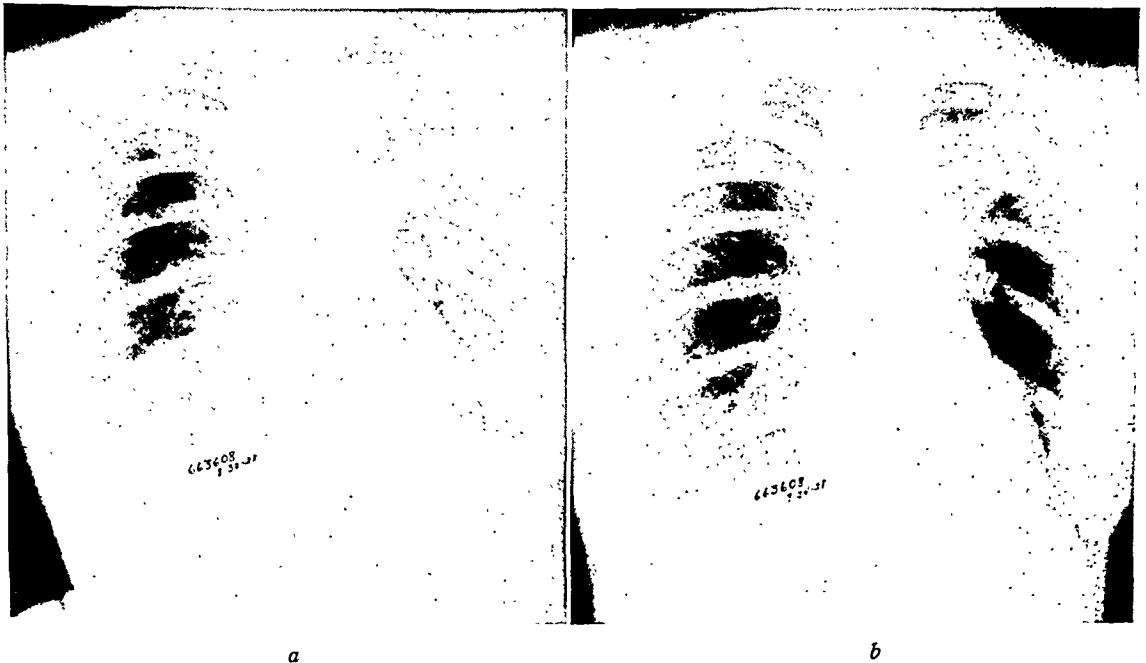


FIG. 2.—*a*, Post-tonsillectomy abscess of ten months' duration; *b*, improvement after two bronchoscopic aspirations.

of life. The youngest patient was aged eighteen months and the oldest seventy-four years. Five patients were in the first decade, seven were in the second, twenty-two were in the third, twenty-nine were in the fourth, twenty-

seven were in the fifth, eleven were in the sixth, two were in the seventh, and two were in the eighth.



FIG 3—*a*, Post influenzal abscess of one month's duration, *b*, after one bronchoscopic aspiration

The conception as to the etiology of pulmonary abscess has undergone a revision since the advent of the bronchoscope. Lukens, in 1926, presented a comprehensive list of possible etiologic factors. He stated his belief that

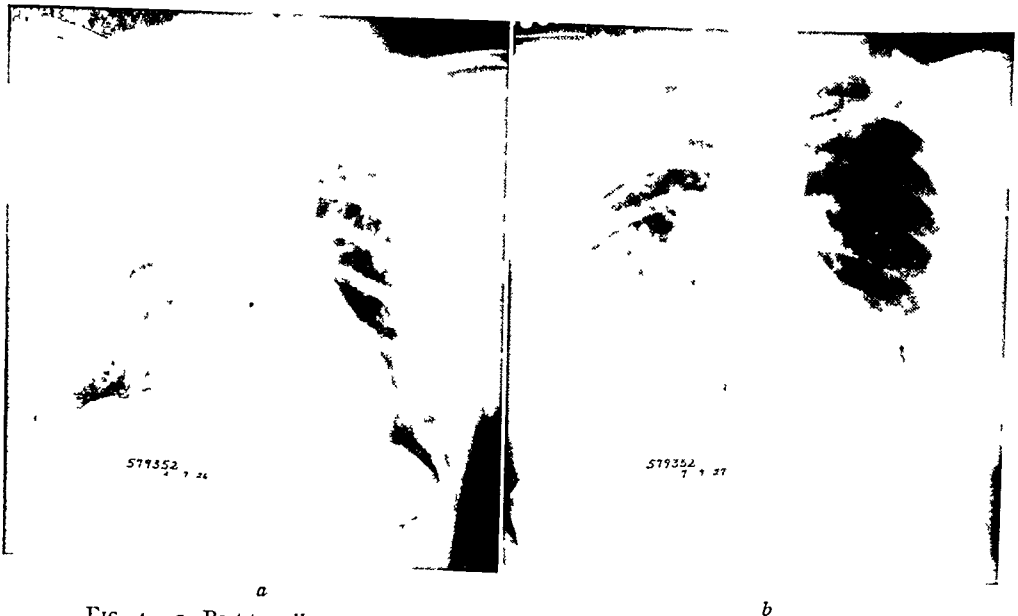


FIG 4—*a*, Post tonsillectomy abscess of three months' duration; *b*, result after two bronchoscopic aspirations

pulmonary abscesses secondary to surgical procedures are more amenable to bronchoscopic treatment than those due to pulmonary disease. In this series of 105 cases, tonsillectomy was considered the etiologic factor in thirty-one

cases, pneumonia in seventeen cases, influenza and colds in twelve cases, general surgical procedures in five cases, foreign body in five cases, dental extraction in five cases, trauma in three cases, and cardiospasm in three cases; in twenty-four cases an etiologic factor could not be determined. Abscess as a result of tonsillectomy constituted the most common cause of pulmonary abscess. This is in agreement with the observations of Lukens and those of Flick, Clerf, Funk and Farrell. The group in which an etiologic factor was not determined is rather large, but many patients were unable definitely to determine the time of onset of symptoms or any possible predisposing cause. The cases listed as due to cardiospasm resulted from material retained in the œsophagus which had been regurgitated into the mouth and apparently aspirated while the patient was asleep.

The duration of pulmonary abscess from bronchoscopic drainage, as Myerson, Jackson, and I have pointed out, is significant in the prospect of cure. It may safely be said that the shorter the duration of the abscess, the better the prospect of cure. This will be more fully illustrated in the consideration of the results obtained in the treatment of pulmonary abscess by bronchoscopic drainage. The duration of the abscess in the 105 cases varied from one week to more than eight years: in twenty-eight cases the abscess had been present less than three months; in twenty-one less than six months; in twenty-six, one year or less; in sixteen, two years or less; in five, three years or less; in three, four years or less; in two, five years or less; in three, six years or less; and in one case eight years.

The situation of the abscess is significant from a technical standpoint as it may influence the accessibility and ease of drainage. Furthermore, the abscess may be single or multiple. The situation of the abscess peripherally or centrally influences treatment. The location of the abscess by means of röntgenograms, general examination, bronchoscopy, surgical procedures and necropsy (when this occurred) was as follows: Right upper lobe, twenty-three cases; right middle lobe, nine cases; right lower lobe, thirty-four cases; multilobular and indeterminate in the right lung, nine cases; left upper lobe, nine cases; left lower lobe, seventeen cases; and multilobular and indeterminate in the left lung, four cases.

Although no particular lobe failed to respond to treatment, the lowest percentage of cures occurred in cases of abscess of the left lower lobe and the right upper lobe. Properly to evaluate the results of bronchoscopic treatment, it is necessary to observe patients for a sufficient length of time. Occasionally, an early favorable response to treatment will not be sustained and the patient will suffer relapse. This is partially counterbalanced by a group of patients that at first fail to respond satisfactorily to treatment, but after a certain period suddenly go on to complete cure. I have been able to trace ninety-eight of the 105 patients, and of these fifty-eight have been under observation from one to five years after completion of treatment. Most of those observed less than a year required some form of treatment other than bronchoscopy.

The results obtained in the bronchoscopic treatment of 105 patients with

pulmonary abscess at The Mayo Clinic from January, 1926, to January, 1931, are as follows: fifty-one patients were cured; eighteen were improved; the treatment of twenty-three was unsuccessful; the results of treatment of seven were questionable, and six died. The term "cured" signifies that all symptoms disappeared completely. "Improved" signifies definite improvement of symptoms. "Unsuccessful" signifies failure to obtain clinical improvement, if the patient failed to coöperate, if it was felt that surgical measures were indicated, and if bronchoscopy was performed as an adjunct to operation. "Questionable results" signifies lack of sufficient data as to the result obtained; however, surgical procedures were not advised in these cases and there was no mortality.

Thus it is shown that of the ninety-eight patients traced, 52 per cent. were cured. As I have pointed out, the shorter the duration of symptoms, the better the result obtained. In twenty-eight of the 105 cases, the abscess had been present less than three months and cures were obtained in 69 per cent. of these.

These results compare favorably with those of Flick, Clerf, Funk and Farrell who reported the results on the treatment of 161 patients treated medically, bronchoscopically or surgically; 50.3 per cent. of the patients recovered. Kernan, in the bronchoscopic treatment of sixty-eight patients, cured thirty-one; four of the patients were still under treatment at the time of the report. Clerf reported the cure of 79 per cent. of patients with pulmonary abscess when treatment was instituted before the third month of symptoms.

In 1928, I reported on the results obtained in a group of nineteen cases of pulmonary abscess; the results were satisfactory in 84 per cent. However, under the classification of satisfactory results was listed not only the cured but the improved patients. With a longer period of observation, I have found that some of those listed as improved have required further treatment.

A review of the patients who died and those who did not respond successfully to bronchoscopic drainage disclosed that five of the patients who died and seven of those who did not improve had empyema associated with the pulmonary abscess. Bronchoscopy was not done with the hope of curing the patient, but rather in conjunction with operation, or if the patient's condition did not permit operation. However, it was deemed advisable that these cases be included in the report, since the pulmonary abscess was the primary disease. There was only one fatality that could be directly ascribed to bronchoscopy; a second death was the result of pulmonary oedema as a result of obstruction due to pressure from mediastinal lymph nodes. By excluding from the group the eleven patients with definitely associated empyema, the percentage of cures would increase to more than 58 per cent.

Severe pulmonary hæmorrhage was the predominating symptom of four patients who did not respond successfully to treatment. It is my impression that patients with pulmonary abscess and associated severe hæmorrhage are less tractable to treatment of all types. Three patients had received previous injections at home to produce pneumothorax and two of them had associated

empyema. Three patients had been operated on unsuccessfully for pulmonary abscess before they came to the clinic. There remained, however, a larger group of cases in which bronchoscopy was unsuccessful in the treatment of uncomplicated pulmonary abscess, and surgical measures were indicated. Whether the percentage of failures can be materially decreased will depend on the alertness with which the disease is recognized after its inception, the variation in the frequency of various etiologic factors and the future improvement of bronchoscopic skill and armamentarium. (Figs. 1, 2, 3, and 4.)

The amount of bronchoscopic drainage necessary in the treatment of any given pulmonary abscess must necessarily vary with existing conditions. However, I feel that when drainage has been well established it is better to give nature a chance to handle the disease properly than to interfere unduly. Just how long a patient should be observed and how frequently bronchoscopy should be done must necessarily vary with the physician's experience. Care, however, must be exercised in not carrying the patient along an unnecessary period of time and thereby add to the difficulties of the thoracic surgeon if bronchoscopic treatment is not successful. In the 105 cases in the series, bronchoscopy was performed once in sixty-five cases, twice in twenty-two, three times in ten, four times in six, and five times in two.

In conclusion, it may be said that bronchoscopy affords another method in the treatment of pulmonary abscess and should be used in conjunction with both medical and surgical measures. At present it affords probably one of the most efficient agents in the treatment of pulmonary abscess.

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# THYROIDECTOMY PERFORMED WITH THE RADIO-KNIFE

(CONCLUSIONS BASED ON 160 OPERATIONS)

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FROM THE JACKSON CLINIC

PREVIOUS to 1930 the radio-knife was tried out repeatedly in various types of operations at the Jackson Clinic, but because it did not offer satisfactory results its use was largely confined to surgery of the genito-urinary tract. With the development of the Grigsby-Grunow unit interest was again revived and, after a year's trial with this machine, the following observations concerning thyroid surgery are offered:

## *Advantages:*

1. The radio-knife is a time-saving factor in thyroidectomy.
2. Hæmostasis is better and with a drier surgical field the operation is facilitated. Fewer forceps are used.
3. In bad-risk cases the reduction in time and the facilitating of the operation are contributing factors in lowering mortality.
4. More thyroid tissue can be removed with less danger to the recurrent laryngeal nerves and the parathyroid glands than with the scalpel.
5. Less catgut is used with improved wound healing.
6. The radio-knife is superior to either the scalpel or the cautery in the treatment of malignancy of the thyroid.
7. It is of particular value in resecting the hyperplastic or exophthalmic type of goitre.

## *Disadvantages:*

1. The radio-knife has not proved satisfactory for the skin incision in my experience.
2. Occasional skin burns have resulted from coagulation too near the surface of the skin.
3. These skin burns, although avoidable, may occasionally occur and result in slight disfigurement of the scar.
4. The tendency to post-operative hæmorrhage is increased.
5. All important vessels must be ligated.
6. The surgeon is dependent on the coöperation of others in using the radio-knife.
7. There is a tendency for the apparatus to fail to function when needed.
8. It is unsatisfactory in resecting large cystic adenomatous goitres.

The radio-knife is a two-edged sword that can easily cause considerable damage unless used with proper regard for its rapid destructive action. Experience is the most important factor, and after one has used it in fifty or

more operations, one gains the necessary confidence to use it smoothly and accurately. While we use the radio-knife as a routine in all goitre operations, we do not use it exclusively but only as an adjunct. Experience has convinced us that a more satisfactory skin incision and a better scar result from using the scalpel. The radio-knife is so rapid in its action that it tends to penetrate the platysma, and causes annoying bleeding from the anterior jugular veins. It has seemed that the scar does not heal as satisfactorily, probably due to the tendency to produce fibrosis.

Early in our experience an occasional skin burn resulted from coagulating vessels too near the surface or in accidentally allowing the coagulating current to come into contact with a hæmostat. These burns are slow to heal like those resulting from diathermy and may leave a disfiguring scar. Experience has tended to eliminate this factor.

In this group of cases there were three post-operative hæmorrhages, a rather high percentage. All of these, I believe, were directly attributable to the use of the radio-knife. None of the vessels were in the gland substance, one was in muscle tissue, one on the surface of the trachea, and one underneath the skin flap. The first patient developed typical symptoms of thyroid hæmorrhage following a rather severe coughing spell four hours after operation. It was necessary to open the wound immediately and ligate a small vessel in the muscle that had been coagulated but apparently not enough. The second patient, who had a hæmorrhage, developed symptoms a few minutes after returning to bed and it was necessary to take the patient to the operating room immediately. On opening the wound a small vessel was found on the surface of the trachea that was oozing in spite of coagulation. As a result of this case, no further attempt has been made to coagulate vessels on the tracheal surface. The third hæmorrhage was due to a vessel oozing slowly from the inner side of the skin flap, causing a hæmatoma that required attention the second day.

We have not attempted to coagulate any important vessels such as the superior and inferior thyroid arteries and veins or any branches of the jugular veins. To be able to coagulate almost all vessels in the gland substance as well as all others with the exceptions mentioned has simplified the operation, eliminated catgut, and has shortened the time of operation.

The use of the radio-knife requires the constant coöperation of the nursing staff and adds another detail to the requirements for teamwork. If a unit could be perfected that might be manipulated entirely by the surgeon, it would be a considerable improvement on the present outfit.

There is a tendency for this unit to get out of order, for a failure of connections to occur, and for certain parts such as the tip holders to break. Further perfection of this apparatus will eliminate annoying interruptions.

In resecting large multiple cystic degenerating adenomas, the radio-knife has not proved so satisfactory in some cases as the scalpel. There is a tendency when cutting through large areas for the tissue to adhere to the knife, so that the latter must be constantly kept clean.

In the May 3, 1930, issue of the *Journal of the American Medical Association*, Mock reported a series of fifteen thyroidectomies performed by an electrosurgical unit. If other reports have appeared in the literature\* since that time I have failed to find them. Mock's conclusions regarding its advantages were as follows:

1. The time of operation is definitely shortened.
2. In every case, even in the most serious with marked cardiac involvement, there has been a complete absence of post-operative shock.
3. A convalescence free from post-operative pain.

Our experience, based on a series of 160 thyroidectomies performed during the past year, does not coincide entirely with the conclusions formed by Mock in this preliminary report. After an almost daily experience with the radio-knife it seems apparent to us that the post-operative reaction in toxic goitre is not particularly influenced. In the bad-risk patients who consist largely of "iodine-fast" cases of exophthalmic goitre, that is, patients who have been kept on iodine so long that they fail to show any pre-operative improvement, we observe the same severe post-operative reaction. Nor is the convalescence in advanced cases of toxic adenoma rendered less stormy.

We do agree with Mock that the time of operation is shortened and as a result a smoother convalescence may follow in some cases. In our experience a certain number of patients still complain of discomfort or pain on swallowing for a day or two, and this factor seems to be governed more by the patient's age, the type and size of the goitre, and the amount of manipulation required in its removal. While it has never seemed to us that post-operative pain was much of a factor in thyroidectomy, certainly less so than after tonsillectomy, it cannot be denied that elderly persons in particular often experience considerable discomfort in swallowing for a day or two.

It is apparent that the problem of eliminating post-operative reaction in extreme cases of toxic goitre is a matter of great importance, and, if there is any method whereby this can be accomplished, it merits careful consideration. We have found that neither the radio-knife nor any other remedy has entirely succeeded in obviating this sequel from thyroid surgery.

In our experience there has been a shortening of the time of operation from five to fifteen minutes, depending upon the number of blood-vessels one would ordinarily have to ligate and also upon the type of goitre. The time factor today, however, does not have the same significance it did a decade ago. With the use of iodine and local anæsthesia together with scopolamine and pantopon these patients experience but little more discomfort in the operating room than they do in bed. Only in the aged, the greatly debilitated, or the extremely toxic cases could the matter of a few minutes' saving in time be considered of much significance.

It is of considerable importance, however, to maintain as dry an operative field as possible and in this respect the radio-knife is a distinct improvement on the scalpel. After reflecting the skin and platysma, one frequently en-

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\* Article by Tinkey in S. G. & O. published since this article was submitted.

counters from one to six small bleeding vessels. It is possible to coagulate five or six such vessels in the time it would take to ligate one. Again, in resecting the gland all clamps except those on the superior and inferior thyroid vessels and lateral veins may quickly be dispensed with by coagulation; likewise, any vessels encountered in the substance of the gland.

One is thus enabled to perform a smoother and speedier operation with less danger to the patient and with greater ease and assurance to the operator. Because the radio-knives may be varied by the use of curved dissectors or even loops it is possible to remove considerably more of the thyroid gland; surgery is performed with greater ease and safety than with the scalpel.

Likewise, in dealing with a very toxic case in which the possibility of a recurrence is suggested by slight tendency of the hyperplastic tissue to revert to colloid, it is possible to remove all but a thin shell of tissue and capsule. This can be done by using the loop and scooping out the tissue, a procedure not possible with a scalpel without endangering the recurrent laryngeal nerves and parathyroid glands.

For many years we have used catgut reels to facilitate ligating the numerous vessels often encountered. The use of these reels has been discontinued and the amount of catgut for the wound to absorb greatly reduced. There has consequently been some improvement in wound healing, 95 per cent. of which are closed without drainage. However, we find as do most surgeons that the majority of the wounds must be probed for a week or more to allow for the escape of a small amount of serum. Occasionally, when a number of vessels have been too vigorously coagulated there may be a discharge of sloughing tissue from the wound for a day or two. This is not so much of a factor as it may sound in the securing of a satisfactory scar and in proper wound healing.

There is no doubt that the radio-knife is the most satisfactory weapon in dealing with accessible malignancy of the thyroid. Mock believes that this method is excellent in these cases because it prevents the escape of carcinomatous cells into the blood and lymphatic streams by its sealing action. Moreover in certain deep cavities not easily accessible to the scalpel it is possible to destroy easily any small areas of malignancy simply by touching them with a hæmostat and in turn touching the latter with the radio-knife coagulating current.

In thyroid surgery the radio-knife is of most value in resecting a gland for exophthalmic goitre. In this type of operation the main objective is to remove as much tissue as possible and still preserve the integrity of the recurrent laryngeal nerves and the parathyroid gland. The radio-knife permits this to a far greater degree of efficiency than the scalpel, because it is possible to hollow out the gland, preserving a very thin lateral, capsular wall and narrow posterior strip protecting these important structures. All the remaining portion of the gland may be scooped out or destroyed by coagulation. A considerable amount of fibrosis results that would certainly hinder development of a recurrence. One might even consider that with the destruc-

tion of so much tissue, hypothyroidism would occur, but there have been none in this series. While we have encountered many types of complications, it has been our good fortune so far to have had only one case of myxœmia following thyroidectomy and that in a recurrent case of exophthalmic goitre.

In resecting a hyperplastic gland we have found the small size loop tip to be very valuable in removing any tissue that may have been left after resection with the straight radio-knife. By placing the index finger behind and posterior to the gland it may be elevated so any small masses of tissue may be easily resected, the loop leaving a very thin layer of tissue above the gloved finger. Considerable care is required not to come too close to the trachea because the heat penetrates rapidly and would not only destroy the tracheal rings but would cause an annoying tracheitis. Also one should avoid touching any instrument that might be in contact with either the trachea or skin, especially if using the coagulating current.

#### SUMMARY

1. Careful consideration of the advantages and disadvantages of the radio-knife in thyroid surgery after a year's experience has convinced us that the advantages considerably outweigh the disadvantages and we shall continue to use it routinely during the coming year.

2. Experience will tend to diminish the number of complications that might occur through its use. In this series of 160 thyroidectomies there were three cases of post-operative hæmorrhage, all of which were controlled successfully.

3. It is possible that the severity of the post-operative reaction in hyperthyroid cases is lessened. The results in this group of cases did not warrant these conclusions.

4. Sufficient time has not elapsed to ascertain the effect of the radio-knife on the prevention of recurrence following thyroidectomy. Because more tissue can be removed or destroyed with a greater degree of safety than with the scalpel, the incidence of recurrence will be decreased.

5. The radio-knife permits the surgeon to perform a smooth, speedy, comparatively dry thyroidectomy, thus increasing the patient's chances of recovery.

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# OBSTRUCTIVE JAUNDICE: ITS SURGICAL ASPECTS\*

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THE most common causes of obstructive jaundice are stone in the common duct, stricture, and tumors in the head of the pancreas, usually carcinoma. Whereas malignant and benign lesions of the duct may occur, these are extremely rare. In a study made in 1930, Marshall found that only four cases of benign tumor and forty-nine cases of primary carcinoma of the extrahepatic bile-ducts had been seen in The Mayo Clinic in twenty years. Of primary importance to the patient with obstructive jaundice is whether the obstruction is due to a nonsurgical lesion within the liver or to a surgical, removable lesion in the bile-ducts. In most instances, it is not difficult to distinguish between these two conditions. The patient with intrahepatic jaundice usually has had no pain, is in good condition considering the depth of the jaundice, or in very poor condition due to the terminal stages of atrophy of hepatic cells. There is bile in his intestinal content as can be determined most accurately by nonsurgical drainage with the Lyon tube. A patient with obstructive jaundice due to stones, in 86 per cent. of cases, will give a definite history of biliary pain or colic. In addition, the jaundice is variable; it usually appears immediately following the colic, and frequently is accompanied by chills and fever. In the presence of carcinoma of the head of the pancreas obstructing the common bile-duct, and of stricture of the common bile-duct, the element of pain is determined by the degree of obstruction and the amount of infection in the biliary passages. In a study of 275 operative cases of obstructive jaundice seen at the clinic, Weir and Partch found that 50 per cent. of patients with carcinoma at the head of the pancreas and 50 per cent. of patients with stricture had had pain associated with jaundice.

*Pre-operative Preparation.*—A period of a few days' observation in the hospital prior to operation is, I believe, of definite advantage to the patient with obstructive jaundice. It gives an opportunity for a regimen of pre-operative preparation to be carried out, and at the same time for the progress of the jaundice to be determined and for the condition of the patient in the presence of painless jaundice to be evaluated. Thus it is possible to determine the necessity of operation.

I believe it is fairly well established that intravenous administration of solution of calcium chloride is of definite value in these cases in prevention of post-operative hæmorrhage. The study of the degree of jaundice by the van den Bergh test gives accurate information concerning the progress

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of jaundice. The value of such knowledge is that it is unwise to operate on patients whose jaundice is increasing unless the condition of the patient forces such operative intervention. If the coagulation time is more than ten minutes, although this is not a contraindication to operation, it is usually an indication that considerable injury has been done to the hepatic cells, and this I believe to be the case if subcutaneous hæmorrhages or petechiæ are present. In such cases, in addition to the solution of calcium chloride, blood transfusion should be given prior to operation and should be repeated as often following operation as is necessary to control the bleeding. To a patient, on whom I have recently operated, who had complete stricture of the common and hepatic bile-ducts, seven transfusions were given in the period of ten days following operation, and only one transfusion was given prior to operation. These transfusions saved her life, however, because on the second and third days following operation, it seemed probable that the bleeding would not cease. The value of intravenous injections of solution of glucose, which usually is given in a concentration of 10 to 20 per cent., has been justly emphasized. Interesting experiences at the clinic in the use of solution of glucose in these cases, beginning in 1921, have shown the efficacy of its use clinically. The early experimental work of Opie, of Mann and of others called attention to its value. More recently, the interesting clinical and experimental studies by Ravdin have borne out contentions concerning its value.

*Surgical Procedures.*—Although general anæsthesia has allowed good exposure of the biliary passages, the increasing safety of spinal anæsthesia has led to its adoption for most patients with obstructive jaundice; the rationale of its use is that it permits perfect relaxation and excellent exposure of the biliary passages which is so important in determination of the site of the lesion and in being certain that it has been completely removed. In addition it lessens the operative reaction by removing the irritating effect of a general anæsthetic on the parenchymatous cells of the liver and kidney. In most instances in which stones exist in the common bile-duct, they may be felt by grasping the duct between the thumb and forefinger. On the other hand, small stones in the ampulla may be missed by external palpation of the duct. The presence of jaundice, or a history of jaundice, chills, and fever, together with increase in the size of the common bile-duct or change in its color from a bluish to a whitish hue, should always lead to opening of the duct for exploration of its interior. Scoops introduced up into the hepatic ducts, and down into the ampulla, usually will bring forth the stones, but the best probe is the finger, and if the size of the duct permits, it is always a good plan to use it to be sure that no stones are overlooked. After removal of the stones from the common bile-duct, whether one elects to use a T-tube or a catheter should depend on the desired duration of drainage of the duct. If there is infection in the liver or in the head of the pancreas, it is best to use the T-tube and to leave it in place for three weeks or longer. Otherwise, a catheter, described by Mayo-Robson as an hepaticus drain, serves admirably to relieve intraductal pressure, and is easily removed on the twelfth day following operation.

If a stricture of the common bile-duct exists, and there is sufficient normal duct above the stricture to allow anastomosis between this normal portion of the duct and the duodenum, a good result may be expected. It is necessary that accurate anastomosis and union of mucous membrane be effected between these two structures; otherwise obstruction will frequently recur at the site of the anastomosis. This procedure, for more than a quarter of a century, has given the best results in the treatment of stricture of the common bile-duct of any type of direct anastomosis. Should the gall-bladder be present, anastomosis between it and the stomach or duodenum can be made and satisfactory results can be expected, provided the stricture is distal to the entrance of the cystic duct into the common bile-duct. However, the gall-bladder usually is not present, because practically all strictures occur subsequently to cholecystectomy, due to injury of the duct.

In some cases in which the stricture is localized, and small in size, a section of the duct containing it can be removed readily, and end-to-end anastomosis can be made between the ends of the duct. I had occasion recently to use this method after I had removed a benign tumor (neuroma) about 1 centimetre in diameter, involving the common and hepatic bile-ducts. When the section of duct containing the tumor had been excised, the stump of the hepatic duct and the stump of the common bile-duct were anastomosed over two small T-tubes. This was done four months ago, and the patient has had a satisfactory course since that time. Similarly, in another case, a stricture was excised, and excision was followed by this type of anastomosis because the stricture was in close proximity to the liver, because a very slight amount of duct remained above the point of stricture and because the stricture was distant from the duodenum, which was difficult to mobilize. The patient has been well, without any further evidence of obstruction, since the operation two years ago. If the stricture involves the entire extrahepatic portion of the common and hepatic bile-ducts, the establishment of an external biliary fistula, which two or three months later can be coned out and transplanted into the stomach or duodenum, has been followed by unexpectedly and unusually good results. Thirteen such cases have been reported in the literature, in seven of which the operation has been performed at the clinic. In the last six years I have operated on twenty-six patients with strictures obstructing the common bile-duct.

Obstructive jaundice, which is the result of tumor at the head of the pancreas, can be relieved by anastomosis between the distended gall-bladder and the duodenum or stomach, the choice depending on the ease of anastomosis and freedom from tension. If the anastomosis is made to the stomach, the presence of bile in the stomach does not produce unusual symptoms. In cases of this type, the intense itching, which in most of these cases is the most constantly troublesome symptom, almost immediately disappears with the release of the obstruction. There is no doubt that some of these tumors at the head of the pancreas are the result of infection and that the relief of the obstruction by cholecystenterostomy gives permanent relief. In a study of 116 patients on whom cholecystenterostomy has been performed at the



clinic, the course subsequent to operation would lead one to suspect that the pancreatic obstruction of the common bile-duct might have, in 15 per cent. of the cases (living longer than five years), been an inflammatory one, although one patient with a pancreatic carcinoma lived comfortably for almost four years. Even if a carcinomatous lesion is the cause of obstruction, the relief of the itching alone warrants the risk of the operation. Moynihan has made the statement that the incidence of suicide among such patients on account of the itching is as high as the operative risk. Noteworthy, also, is the fact that operation on such jaundiced patients allows thorough exploration of the biliary passages, and not infrequently a stone in the common bile-duct is unexpectedly found as the cause of the obstruction.

In a recent study, Weir and Partch found that nineteen of 104 patients with stones in the common bile-duct had painless onset of jaundice and that seventeen of these 104 patients had not had pain at any time. If jaundice is extreme, I believe that cholecystenterostomy can be done more safely in two stages than in one stage. In the first operation, the gall-bladder is drained, and twelve or fourteen days later anastomosis between the gall-bladder and the stomach or duodenum is effected. If the jaundice is not deep, and the condition of the patient permits it, there is no reason why cholecystenterostomy cannot be done in one stage. It has been my custom, when performing the operation in one stage, to make the anastomosis by suture, but when I have carried out the procedure in two stages, I have found a small Murphy button to maintain a constant lumen and to prevent even its temporary closure by inflammation or œdema. The heavy end of the Murphy button always should be placed on the duodenal or gastric side of the line of anastomosis to lessen the possibility of its dropping into the gall-bladder. That cholecystenterostomy can be carried out with a fair margin of safety is indicated by the fact that in 1929, cholecystenterostomy was performed at the clinic on ten deeply jaundiced patients for relief of obstructive jaundice due to tumors at the head of the pancreas, and all of these patients recovered and returned home. The statistics for the year 1930 will not be available until next month, but my impression is that a similarly low rate of mortality has been maintained.

*Complications.*—The complications which occur following operations on patients with obstructive jaundice are hæmorrhage and renal and hepatic insufficiency. Of great importance in lessening the incidence of post-operative hæmorrhage is the selection of the proper time for operating and the pre-operative use of some means of assisting in the coagulation of the blood. A successful outcome in such cases is absolutely dependent on the relief of the obstruction. When patients fail to recover following removal of stones from the common bile-duct, it will be found that in most instances stones have been overlooked. Such overlooked stones can cause recurring obstruction, deepening jaundice with possibly hæmorrhage, and renal and hepatic

insufficiency as terminal features. The same necessity for complete relief of obstruction is involved in operating on patients with strictures and tumors at the head of the pancreas. On a few occasions, I have seen patients following cholecystenterostomy for tumors at the head of the pancreas almost lose their lives from temporary obstruction at the anastomosis due to inflammation and œdema. The corollary of this is that if anastomosis is made by suture, the opening must be as large as possible.

I believe it is worth while to administer 10 per cent. solution of glucose intravenously to jaundiced patients subsequent to operation, as often as such treatment is indicated. At the time that the needle is inserted into the vein for the injection, a small amount of blood may be removed for determination of coagulation time, change in the degree of jaundice, and determination of the concentration of urea in the blood. Occasionally, there will be reflux of duodenal secretions into the common bile-duct, and these will be discharged through the tube drain that has been placed in the common bile-duct. The diagnosis of this condition is usually evident when more than 400 or 500 cubic centimetres of bile are drained over a period of twenty-four hours, especially if the bile is light in color due to the dilution of the bile by duodenal secretion. Methylene blue given by mouth appearing in the draining fluid makes the diagnosis certain. Clamping of the tube frequently will prevent the loss of much of this fluid. This is especially true if a T-tube is used. At the same time, an intake of fluid must be maintained which is greater than the total amount of fluids lost, or else dehydration toxæmia will occur.

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# INTERMITTENT JAUNDICE DUE TO NEUROMA OF CYSTIC AND COMMON BILE DUCTS\*

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INTERMITTENT obstructive jaundice due to the formation of tumor of the bile ducts is comparatively rare. Marshall, in 1930, found that only four cases of benign tumor and forty-nine cases of primary carcinoma of the extrahepatic bile ducts had been seen in The Mayo Clinic in the last twenty years. Rolleston and McNee, in 1929, recorded 112 cases of carcinoma of the ducts exclusive of the growths in the ampulla, and of only ten cases of benign tumors. Of these tumors the benign, although much more rare than the malignant, lend themselves to surgical cure and afford the patient assurance that recurrence or metastasis will not occur. A twofold interest is found in these cases of intermittent obstructive jaundice due to a benign tumor of the extrahepatic bile ducts, of which the following is an example.

REPORT OF CASE.—A woman, aged fifty-five years, registered at the clinic September 30, 1930, complaining of pruritus and jaundice of two and a half weeks' duration. At the age of thirty years a series of typical attacks of colic of the gall-bladder began; they were not associated with jaundice. Ten years before admission cholecystectomy and appendectomy had been performed elsewhere. A biliary fistula persisted. Two temporary closures of the fistula were followed by jaundice; the final closure occurred eighteen weeks after operation and the patient remained well for five years. Five years afterward deep jaundice developed, which was essentially painless and was associated with anorexia and pruritus. The jaundice disappeared after five weeks, to reappear one and a half years later and to last five or six weeks. This second attack of jaundice as well as the third, which occurred a year before admission, was accompanied by severe prostration, loss of strength and weight, chilly sensations, and slight fever. The last attack began at night in the right upper quadrant two and a half weeks before admission with discomfort which awakened the patient from sleep. Vomiting relieved the distress. Jaundice and pruritus appeared two days later. The appetite remained fair and the digestion good. The stools became clay-colored and the urine dark.

The patient was 5 feet, 2 inches tall and weighed 126 pounds. She had lost 20 pounds in the last five years, but appeared to be well nourished. She was markedly jaundiced and her skin had been diffusely excoriated by scratching. Nodules were not found along the course of the nerves suggestive of von Recklinghausen's disease. The liver was slightly enlarged and firm. The specific gravity of the urine was 1.021; it was acid in reaction, did not contain sugar, but a moderate amount of bile, and an occasional erythrocyte and leucocyte in the high-power field. The test of urobilin was positive. The percentage of hæmoglobin was 80; erythrocytes numbered 3,950,000 and the leucocytes 7,100. The coagulation time by the Lee and White method was 6

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minutes and 30 seconds. The serum bilirubin was 11.5 milligrams and the van den Bergh reaction was direct. The stools were negative for bile with the Schmidt test. Clot retraction was slight at the end of one hour and complete at the end of two hours. The fragility test gave normal resistance. The blood urea was 22 milligrams for each 100 cubic centimetres. Repeated duodenal drainage showed a trace of bile in the contents.

During the patient's stay in the hospital before operation normal temperature and pulse persisted. The concentration of serum bilirubin fell gradually and October 8, the reading was 7.1 milligrams. The coagulation time increased to ten minutes, but following transfusion October 9, and intravenous administration of 10 per cent. calcium chloride in amounts of 5 cubic centimetres, it dropped to seven minutes. A diagnosis was made of intermittent and partial obstruction of the common bile duct. The history of cholecystectomy for cholecystitis with stones and the intermittent appearance of jaundice over a five-year period indicated stones as the cause of the obstruction. On the contrary, the initial appearance of jaundice after operation and its painlessness indicated stricture. The unusual feature was the long interval between attacks.

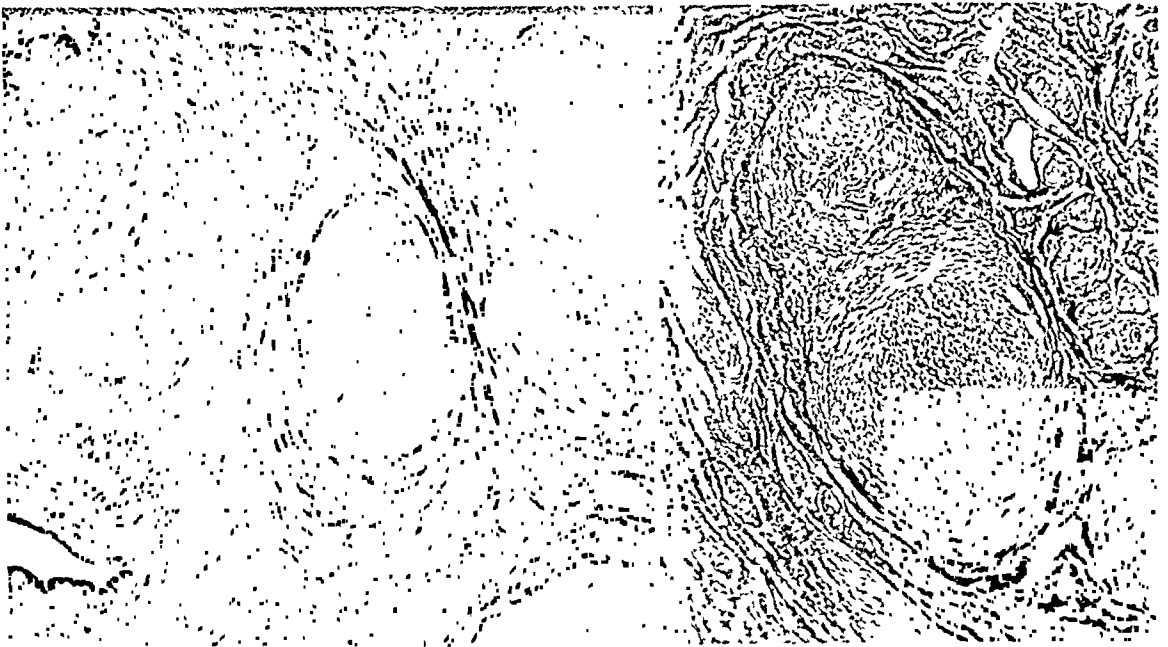


FIG. 1.—Sheath neuroma of the common and cystic ducts. Interlacing cellular strands covered by fibrous sheaths in a groundwork of connective tissue surrounding the cystic duct (van Gieson's stain).

FIG. 2.—Sheath neuroma of the common and cystic ducts. Cross section of a cellular strand ensheathed by well-developed fibrous capsules (van Gieson's stain).

October 10, 1930, operation was performed. There was a solid lesion in the middle portion of the common bile duct approximately 1 centimetre in diameter, and obstructing the duct. This portion of the duct was excised. A common-duct probe and scoop could be passed through the lower end of the duct into the duodenum. The two ends of the stumps of the hepatic duct were sutured to the lower end of the common bile duct over two small T-tubes, interrupted sutures of silk being used in the anastomosis. Satisfactory anastomosis between the ducts was accomplished.

The patient's post-operative convalescence was uneventful, and she was allowed to return home, November 3. The incision healed except for the sinus the T-tubes occupied. She was in excellent condition. The T-tubes have remained closed, allowing bile to pass into the external limb of the duodenum. She continues to be in excellent condition (January 8, 1931) and will return to the clinic within a few weeks for the removal of the T-tubes.

The specimen removed at operation measured approximately 1.5 by 1 by 0.75 centimetres. It was firm, and on cross section a central canal whose walls were continuous

with the attached portion of the common bile duct could be traced three-fourths of the way to the free end of the mass. Sections were stained with hæmatoxylin and eosin, van Gieson's stain, and by silver impregnation methods for axis cylinders. The central canal, observed grossly and microscopically, had the appearance of the cystic duct. Chronic inflammatory changes (lymphocytes and fibroblastic reaction) were present in the mucosa. Mucous glands were seen. Two types of tissue composed the remainder of the tumor: Connective tissue, and large and small bundles of tissue which ran in all directions. The many interlacing strands gave an unusual plexiform arrangement. The connective tissue had an adult appearance and did not contain evidence of inflammatory reaction seen in the mucosa. The interlacing bundles of tissue were composed of numerous elongated cells lying parallel to the long axes of the bundles, often assuming the wavy arrangement characteristic of nerve tissue; they stained yellow with the picric acid of van Gieson's stain. The nuclei stained brown. Palisade arrangement of the nuclei, interlacing fibrils, or foam cells were not present. Usually the bundles had heavy sheaths of a mixture of young and old connective-tissue cells. Red- or pink-staining connective fibrils were not present inside the bundles. Silver impregnation showed swollen fragments, which were difficult to recognize as axis cylinders, although they gave fairly characteristic staining reactions. The tumor had an unusual structure. Its classification was difficult because of lack of data on a similar tumor. It did not correspond to the acoustic or von Recklinghausen's neurofibromas; moreover, it was solitary. Rosettes such as were described by Stout in his case of tumor of the ulnar nerve were not observed nor was the peculiar cellular arrangement of the sheath neuroma of the Gasserian ganglion described by Learmonth and Kernohan present. There seemed to be an excessive overgrowth of the sheath cells which are normally present in the sympathetic nervous system, accentuating the numerous small nerve bundles which normally lie in the connective tissue around the cystic duct. The term sheath neuroma has been suggested by Kernohan for the tumor in spite of the fact that it is dissimilar to one previously observed by him. He explained the difference on the basis that in this case the tumor is of the sympathetic nerve trunk and not of the sensory ganglion.

The neuroma in this case is not only rare but its situation is unusual. Cysts of the common bile duct,<sup>5</sup> adenofibromas of the cystic ducts,<sup>8</sup> and papillomas of the cystic and common bile ducts have been reported.<sup>5, 7, 9</sup> Fibromas,<sup>1, 4</sup> adenomyofibromas,<sup>11</sup> lipomas,<sup>3, 12</sup> and hydatid cysts<sup>2</sup> are other types of benign tumors. The types seem to be almost as numerous as the tumors themselves. The explanation of the obstruction by external pressure of the tumor is of interest. W. J. Mayo found the same explanation feasible for his two cases of adenofibroma of the stump of the cystic duct which similarly produced intermittent obstructive jaundice with symptoms of cholangitis. The symptoms of obstruction of the common bile duct due to benign tumors are indistinguishable from those due to stone, especially if the stone is silent, to partial stricture secondary to surgical accidents, or to the formation of scar from pressure of the stones. The progressive course and at times the blood in the duodenal contents will serve to distinguish benign from malignant stricture. Pain and signs and symptoms of coëxisting infection may or may not be present. The benign nature of the lesion may be suspected in similar cases. Its rarity will not encourage one to venture a definite diagnosis.

# JAUNDICE FROM NEUROMA OF BILE DUCT

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## ASYMPTOMATIC COMMON-DUCT STONES\*

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THE classical symptoms caused by the presence of stones in the common and hepatic bile-ducts are well known. Briefly, these are pain, followed by varying intensities of jaundice, which may be constant or remittent, the intermittent fever of Charcot,<sup>1</sup> the absence of bile from the stools and the presence of bile pigment in the blood serum and urine, sometimes associated with hepatic insufficiency, recognized clinically as cholæmia, complete the clinical picture. This syndrome may vary not only in degree but in the complete absence of one or another of the diagnostic criteria. Pain may be entirely lacking, estimated at about 5 per cent. of the cases in a report by Jordan,<sup>2</sup> of the Mayo Clinic. The intermittent fever and chills, a manifestation of secondary infection of both the intra- and extra-hepatic biliary ducts collectively grouped under the term cholangitis, is rather a late manifestation of calculous biliary obstruction than an early one, and finally jaundice, the outstanding diagnostic aid to the recognition of common-duct stones may be entirely absent.

It is evident, therefore, that in some measure we must reshape our conception of the symptomatology of choledocholithiasis to include a number of cases which do not answer to the classical description. I have grouped these under the heading of asymptomatic or latent common-duct stones.

### CASE REPORTS (*abstracted*)

CASE I.—No. 279881, B. S., female, aged twenty-eight, admitted May, 1927, to the Surgical Service of Dr. A. A. Berg with a history dating back three years, consisting briefly in sharp intermittent attacks of pain in the right upper quadrant, radiating to back and shoulders. There were accompanying gastro-intestinal disturbances. Patient had never noticed jaundice, clay-colored stools or any change in the color of her urine. There had been no chills or fever. Urine examination upon admission was negative for bile. Van den Bergh test: direct—negative, indirect—1 to 500,000.

*Operation and Findings.*—Operator.—Dr. A. A. Berg. A small, shrunken and thickened gall-bladder containing stones was found. Typical cholecystectomy from above downward. Common duct probed; no apparent obstruction encountered. Further palpation, however, revealed a small stone in the common duct at the papilla of Vater. Choledochotomy with removal of stone. Closure of duct. Patient made an uneventful recovery and was discharged well, eighteen days after operation.

CASE II.—No. 276171, S. K., female, aged thirty-seven, entered hospital upon the Surgical Service of Dr. A. A. Berg in June, 1927, with a history of pain in the right upper quadrant, coming on in attacks for two years prior to admission. These seizures of pain were becoming more frequent and were increasing in intensity. No jaundice, change in color of stools or urine noted at any time since onset. No chills or fever.

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\* Read before the Surgical Section of the Academy of Medicine of New York, January 2, 1931.

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Physical examination revealed no clinically discernible jaundice. Urine was negative for bile. Van den Bergh test showed a direct negative reaction; indirect 1 to 400,000.

*Operation and Findings*.—Operator.—Doctor Klingenstein. Gall-bladder distended, containing numerous small and large calculi. Palpation through foramen of Winslow revealed the common and hepatic ducts to contain myriads of small calculi extending from the papilla of Vater into the hepatic ducts. Removal of stones and choledochostomy with reconstruction of common bile-duct over a tube. Patient discharged well, twenty-three days after operation.

CASE III.—No. 294566, G. B., female, aged thirty-seven, admitted to the Surgical Service of Doctor Lewisohn, September, 1928, with a history of pain in the right upper quadrant, increasing in severity, of one year's duration. Has noted no jaundice, chills or fever. Physical examination showed no icterus. Urine negative for bile. Van den Bergh test of blood serum yielded a negative direct reaction and an indirect concentration of 1 to 333,000.

*Operation and Findings*.—Operator.—Doctor Lewisohn. Gall-bladder chronically inflamed, thickened, containing stones. One stone palpated in the common duct near the papilla of Vater. Procedure.—Cholecystectomy followed by choledochostomy with removal of stone from the supraduodenal portion of the common duct. Patient made an uneventful recovery; discharged twenty days after operation.

CASE IV.—Nos. 263972 and 301897, S. Z., female, aged thirty-four, admitted for first time February, 1926, with history of epigastric pain, radiating to both hypochondria and back, relieved by morphine. At this time it was noted that patient was gravid. Urine negative for bile. Van den Bergh test, direct—negative; indirect—1 to 400,000 or .25 milligram per 100 cubic centimetre. Second admission to the Surgical Service of Dr. C. A. Elsberg in April, 1929, for frequent attacks of severe right upper quadrant pain accompanied by nausea and vomiting. Has never been jaundiced. Urine negative for bile. Van den Bergh test, direct—negative; indirect—1 to 500,000.

*Operation and Findings*.—Operator.—House Surgeon. Gall-bladder contained numerous stones. Cholecystectomy from above downward. After the ablation of the gall-bladder, numerous stones were then removed from the common duct through the divided cystic duct. Calculi ranged in size from 1 to 4 milligrams. Patient discharged well twenty-four days after operation.

CASE V.—No. 299740, J. D., female, aged fifty-six, admitted to the Surgical Service of Dr. A. A. Berg in February, 1929, with a fourteen-year history of typical attacks of gall-stone colic, at six-month intervals. Never noted chills, fever, jaundice or clay-colored stools. Urine negative for bile. Van den Bergh test, direct—negative; indirect—1 to 500,000.

*Operation and Findings*.—Operator.—Dr. A. A. Berg. Chronically inflamed gall-bladder filled with faceted calculi. Stones in common duct of various sizes extending up into hepatic ducts. Common duct noted to be dilated. Procedure—choledochostomy with removal of stones. Uneventful convalescence. Patient discharged well, twenty-six days after operation.

The cases (*vide supra*) which answer to this description present themselves with a typical history of gall-stones usually accompanied by colic, but which at no time in the clinical course have noticed jaundice, clay-colored stools or bile in the urine. Physical examination of these patients has revealed no clinical evidences of icterus and the chemical analysis of the blood for bile pigments—the Van den Bergh test, and the examination of the urine for bile prior to operation have revealed no evidence of increased bile pigments in either the urine or the blood serum. I have left out of consideration a group of cases, not inconsiderable, who, prior to



admission, have noted evanescent jaundice, which evidenced itself at the end of an attack of biliary colic, and another group of patients who, definitely jaundiced while under observation, lose their icterus prior to operation. I have included only those cases in whom there was no clinical or laboratory data sufficient to warrant the supposition that the potentialities for common-duct obstruction existed. It is impossible to determine whether at some time during the course of the disease latent jaundice as described by Bernheim<sup>3</sup> could have been demonstrated.

In reviewing 82 choledochotomies for calculus performed on the ward services of Mount Sinai Hospital during the past five years, we encountered five cases answering the above criteria. A little over 6 per cent. of our cases of common-duct stones could therefore be classified as asymptomatic or latent. Different authors have reported varying percentages of asymptomatic choledocholithiasis: Mayo-Robson,<sup>4</sup> 1 per cent; Jordan,<sup>5</sup> from the Mayo Clinic, 13.2 per cent; F. Rossi,<sup>6</sup> a little over 10 per cent. Clute,<sup>7</sup> recently from the Lahey Clinic, reports as high as 39 per cent. of patients with common-duct stones without jaundice. Kehr,<sup>8</sup> as far back as the beginning of the present century, stated that "jaundice can be completely wanting, despite a large stone in the choledochus." It seems reasonable, also, that a certain percentage of patients with asymptomatic gall-stones have a concomitant silent choledocholithiasis, as evidenced by a patient who recently came to necropsy, succumbing to an intercurrent disease, with four large common-duct stones. I have not reviewed the autopsy material to ascertain how common this finding is. It is suggestive, although not proven, that these stones occupied the duct during life. Manipulation, relaxation of the cystic duct after death, may account for their post-mortem position, but is not probable.

An analysis of our cases reveals the following: All occurred in women. I do not believe that one should conclude therefrom that the condition is limited to the female sex, but rather because of the small series, and the preponderance of women having gall-stones, the circumstance is accidental. The ages varied between twenty-six and fifty-six, four of the cases occurring during the second and third decades. The duration of the symptoms of gall-stones prior to operation varied between one and fourteen years; the mean duration was about six years.

In all cases except one the multiplicity of the calculi as well as the difference of sizes speak against the possibility of the stones being forced through the cystic duct into the common during the manipulations incident to cholecystectomy. Quite surprisingly, the common duct was dilated in only one case (Case V). In Case II, in which the choledochus as well as the hepatic ducts were completely filled with small calculi, the duct was of normal size. In no case was the bile frankly purulent. In no case did the urine contain bile, and the Van den Bergh test was well within normal limits.

It would not seem that the duration of gall-bladder symptoms influences the possibility of stones being found in the choledochus. They were found

in patients with short as well as long histories. In all cases the gall-bladder was also the seat of stone formation, containing numerous gall-stones of varying sizes. The number of stones in the common duct varied from one solitary stone as in Cases I and III to numerous stones occupying almost the entire extrabiliary duct system as in Cases II and V. The size also was not constant; in Cases I and II they were small, in Case V large and faceted, bespeaking a long residence in the common duct. In two, Cases I and III, the stones were situated at the papilla of Vater; in two, Cases II and V, the stones were multiple and occupied the entire duct system extending well up into the hepatic duct. In one case, the position of the stone was not mentioned in the history. In all cases except one, incision into the common duct was necessary for their removal. In one case, the stones were milked upward and were extracted through the stump of the divided cystic duct.

It is interesting to speculate why certain cases of common-duct stones should present no symptoms. In no case was there a biliary intestinal fistula to account for the absence of jaundice. The possibility of hepatic insufficiency with lessened bile formation cannot be proven in these cases, for no liver-function tests were undertaken. It would prove interesting to adopt functional liver tests as a routine in gall-bladder cases to determine if cases with asymptomatic common-duct stones show dye retention. Another explanation, adduced by the experimental work of Mann,<sup>9</sup> who showed that the dilatation of the extrahepatic biliary tract and gall-bladder delayed the advent of jaundice in common-duct obstruction, would seem only to hold good in those cases with dilated common ducts. In this series only one case could be explained on this basis. It would seem that the best explanation is one of incomplete obstruction of the duct, due to either initial dilatation or the small size of the calculus.

The ever-increasing literature, dealing with the jaundiced patient as a bad surgical risk and as demonstrated by Colp,<sup>10</sup> who reviewed our cases in 1927, and by Walters,<sup>11</sup> of the Mayo Clinic, makes it imperative for the surgeon to be alive to the possibility of overlooking common-duct stones before the advent of jaundice or infections, both of which increase the morbidity and mortality of the operation. It is of interest to speculate whether in these cases jaundice would have supervened. In one case, Case II, who has since been re-operated upon for recurrent common-duct calculi, jaundice was present at the second operation. It is assumed in this case that we are dealing with one of intrahepatic cholelithiasis and her subsequent history would tend to substantiate this opinion. It is impossible to estimate how many patients pass common-duct calculi. It unquestionably occurs as the literature is replete with instances of large stones having been passed by rectum in the absence of cholecysto-intestinal fistulæ. It must be assumed, however, that this is uncommon even in the presence of diminishing jaundice and absence of temperature. Our records show several cases operated upon after the subsidence of the evidence of complete obstruction, who still revealed common-duct stones. On the other hand, it has been every surgeon's

experience to explore patients with a history of common-duct calculi only to find a dilated common duct without stones. These cases can be explained only on the basis of a passed stone or of a cholangitis.

From the above series of cases and the experience of other surgeons, it is evident how difficult it is to be certain before operative interference of the presence of common-duct stones. Nor is it always easy to be sure of their presence during exploration or during operations upon the gall-bladder, but it is certain that if the surgeon keeps their possible presence constantly in mind, the possibility of his overlooking them will be lessened. Palpation alone, except in the large-size stones, is not always reliable. This is particularly true of the small stone situated at the ampulla of Vater. The head of the pancreas, through which the common duct must be palpated in this location, particularly if thickened, presents an obstacle to a really accurate palpation. Exploration of the common duct by means of a probe introduced through the cystic duct is not only very difficult at times but also easily misleading. It has been everyone's experience to have failed to enter the common duct through a narrow or strictured cystic duct.

The Heisterian valves also present a barrier to the probe which, at times, it is difficult to overcome. Having been fortunate enough to enter the common duct with a probe, it is furthermore difficult to be sure that the probe has really entered the duodenum. At times, the probe pushes the papilla of Vater ahead of it so that one is falsely impressed that the probe has entered the intestine. Unless one actually sees the blunt end of the probe entirely free, presenting itself into the anterior duodenal wall, one cannot be certain of its having traversed the papilla.

How far is one justified in advocating choledochotomy on the basis of asymptomatic stones? Clute,<sup>7</sup> in a recent article reviewing cases from the Lahey Clinic, revealed that more than one-third of the cases operated upon for gall-bladder diseases were subjected to common-duct exploration, increasing thereby the number of common-duct stones encountered from almost 8 per cent. to almost 18 per cent. The author does not regret the exploration in those cases in which stones were not found, but rather is proud of the increased number of stones unearthed in the common duct incident to wider indications for exploration.

It is well recognized that only in exceptional circumstances do stones form in the bile-ducts. Authentic cases of intrahepatic cholelithiasis, as those reported by Beer,<sup>12</sup> Lewisohn,<sup>13</sup> and Judd,<sup>14</sup> are exceptions. Any case of recurrent common-duct stones is one possibly overlooked at the original operation. In all cases, in spite of vigorous attempts to free the ducts of calculi, it may be difficult to entirely clear the bile passages of the finer particles of detritus, which, in combination with the residual infection, may form the basis of new stone formation. These cases, however, form only a small group. Most cases that require re-exploration are on the basis of overlooked stones in the common duct.

Exploration of the common duct should not materially increase the mor-

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talities of gall-bladder surgery. Clute's<sup>7</sup> recent statistics confirm this. In the presence of dilatation of the duct, a history of jaundice after attacks of gall-bladder colic, the common duct deserves exploration. The possibility of overlooking calculi in cases which do not present so evident indications as the series just reviewed and which have been confirmed by others, should impress the operator with the potentialities of common-duct stones in all cases of cholelithiasis. Only in this way will sufficient common-duct stones be explored to safeguard the patient against the complications of this condition with its attendant high surgical risks.

### SUMMARY AND CONCLUSIONS

1. A series of asymptomatic common-duct stones without jaundice is presented and discussed.

2. Every case of cholelithiasis is potentially one of choledocholithiasis.

3. A recognition of common-duct stones in those patients without symptoms will safeguard a certain number against the complications of biliary-duct obstruction with its attendant high surgical mortality.

The author wishes to thank Drs. A. A. Berg and Charles A. Elsberg for permission to report cases occurring upon their services.

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# THE VALUE OF EARLY OPERATION FOR ACUTE CHOLECYSTITIS\*

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MANY leading surgeons of this country advise a policy of watchful waiting in acute cholecystitis. Others, equally well known, urge prompt operation without any unnecessary delay. If one group is right, it is evident that, in most instances, the other group must be wrong.

A careful analysis of a sufficiently large group of cases ought to furnish some definite evidence pointing in one direction or the other.

The following statistics are presented with the hope that they may be of value in forming a decision when it becomes necessary to advise a patient suffering from acute cholecystitis either to have an early operation or to postpone it to a future date.

These cases were found in the bound volumes in the record room of the Methodist Episcopal Hospital. They were signed out by the Attending Surgeon as acute cholecystitis. The diagnosis, in a few instances, is open to question, but it seemed best to avoid any editing by the reviewer.

## ACUTE CHOLECYSTITIS

A report of 198 consecutive cases operated upon at the Methodist Hospital, Brooklyn, between December 12, 1919, and August 5, 1928. There were fifty-six cases during this same period that were not operated upon.

There were twenty cases operated upon within forty-eight hours of the onset of acute symptoms (Group A). There were 178 cases with operation more than forty-eight hours after the onset of acute symptoms (Group B).

| <i>Statistics</i>             | <i>Group A</i>                   | <i>Group B</i>             |
|-------------------------------|----------------------------------|----------------------------|
| Deaths.....                   | 1 (5%)                           | 11 (6.2%)                  |
| Females.....                  | 15 (75%)                         | 141 (79%)                  |
| Previously pregnant.....      | 10 (50%)                         | 101 (56%)                  |
| Males.....                    | 5 (25%)                          | 37 (21%)                   |
| Average age.....              | 43.5 years                       | 43.5 years                 |
| Average time in hospital....  | 19.5 days (Death exclud. 2 days) | 26.4 days                  |
| Longest time in hospital....  | 28 days                          | 79 days                    |
| Shortest time in hospital.... | 14 days (Exclud. death 2 days)   | 13 days (Home sick 5 days) |
| Average number of dressings   | 4½                               | 10½ (10.44%)               |
| Burst wounds.....             | 0                                | 5                          |
| Post-operative complications  | 1 (5%)                           | 36 (18%)                   |

## OPERATIONS

|  | <i>Group A</i> | <i>Group B</i> |
|--|----------------|----------------|
| Cholecystectomy, drainage specified..... | 13             | 101            |
| Cholecystectomy.....                     | 5              | 43             |
| Cholecystostomy.....                     | 2              | 32             |

\* Read before the Medical Society of the County of Kings, New York, February 17, 1931.

# EARLY OPERATIONS ACUTE CHOLECYSTITIS

## OPERATIONS (*Continued*)

|                                      | Group A | Group B |
|--------------------------------------|---------|---------|
| Choledochostomy.....                 |         | 7       |
| Excision of biliary fistula.....     |         | 1       |
| Drainage of liver abscess.....       |         | 1       |
| Resuturing of wound.....             |         | 7       |
| Iridectomy.....                      |         | 1       |
| Transfusions.....                    |         | 2       |
| Release of intestinal adhesions..... |         | 1       |
| Jejunostomy.....                     |         | 1       |
| Appendectomy.....                    |         | 25      |
| Oöphorectomy.....                    |         | 2       |

## PATHOLCGY FOUND IN GALL-BLADDER

|  | Group A | Group B |
|--|---------|---------|
| Distended, with stones.....                    | 11      | 38      |
| Acutely inflamed, with stones.....             | 4       | 51      |
| Acutely inflamed, no stones mentioned.....     | 3       | 27      |
| Chronically inflamed, with stones.....         | 0       | 19      |
| Chronically inflamed, no stones mentioned..... | 0       | 14      |
| Gangrenous gall-bladder.....                   | 2       | 10      |
| Stones in common duct.....                     | 0       | 5       |
| Abscess of gall-bladder.....                   | 0       | 15      |
| Ruptured gall-bladder.....                     | 0       | 7       |
| Other acute pathology—                         |         |         |
| Acute pancreatitis.....                        | 1       | 2       |
| Liver abscess.....                             |         | 1       |
| Abscess outside gall-bladder.....              |         | 3       |
| Adhesions outside gall-bladder, many.....      |         | 1       |
| Local peritonitis.....                         |         | 2       |
| Fistula—gall-bladder, duodenum.....            |         | 1       |
| Fistula—gall-bladder, stomach.....             |         | 1       |

## POST-OPERATIVE COMPLICATIONS

|                                | Group A | Group B |
|--------------------------------|---------|---------|
| Suppurative parotitis.....     | 1       | 0       |
| Biliary fistula.....           |         | 1       |
| Duodenal fistula.....          |         | 1       |
| Lobar pneumonia.....           |         | 9       |
| Bronchopneumonia.....          |         | 1       |
| Pneumothorax.....              |         | 1       |
| Lung abscess.....              |         | 1       |
| Wound rupture.....             |         | 5       |
| Wound infected—no rupture..... |         | 4       |
| Phlebitis.....                 |         | 3       |
| Gluteal abscess.....           |         | 1       |
| Decubitus ulcer.....           |         | 1       |
| Acute glaucoma.....            |         | 1       |
| Herpes zoster.....             |         | 1       |
| Septicæmia.....                |         | 1       |
| Typhoid fever.....             |         | 1       |
| Myocardial failure.....        |         | 5       |
| Intestinal obstruction.....    |         | 1       |
| Secondary hæmorrhage.....      |         | 1       |

## ANALYSIS OF DEATHS

*Group A*

| <i>No.</i>     | <i>At home before<br/>operation</i>     | <i>In hospital before<br/>operation</i> | <i>Pathology</i>                           | <i>Operation<br/>Time</i> | <i>Cause of death</i>                          |
|----------------|---|---|--|---------------------------|--|
| 177            | 30 hours                                | 3 hours                                 | Acute cholecystitis<br>Acute pancreatitis  | 105 minutes               | Pancreatitis                                   |
| <i>Group B</i> |   |   |  |                           |  |
| 71             | 4 days                                  | 4 days                                  | Cholecystitis; no stones                   | 50 minutes                | Pneumonia or pulmonary embolus                 |
| 76             | 10 days                                 | 1 day                                   | Abscess gall-bladder and liver             | 30 minutes                | Delay at home                                  |
| 86             | 14 days                                 | 1 day                                   | Cholecystitis; stones                      | 90 minutes                | Pneumonia                                      |
| 119            | 7 days                                  | 9 days                                  | Cholecystitis                              | 30 minutes                | Liver abscess                                  |
| 132            | 15 months                               | (Wrong filing)                          | Chronic cholecystitis                      | 50 minutes                | Septicæmia                                     |
| 138            | 21 days<br>Chart face "Acute"           | 5 days                                  | Empyema gall-bladder                       | 60 minutes                | Delay at home, peritonitis; myocardial failure |
| 168            | Vomiting<br>2 months                    | 1 day                                   | Cholecystitis; stones                      | 90 minutes                | Cardiac dilatation or embolism                 |
| 176            | Epigastric distress<br>3 months, 1 week | 15 hours                                | Stones in common duct; pancreatitis        | 160 minutes               | Long operation; complicated pathology          |
| 200            | 11 days                                 | 2 days                                  | Distended gall-bladder; acute pancreatitis | 95 minutes                | Pancreatitis                                   |
| 225            | 1 month                                 | 1 day                                   | Atrophic gall-bladder; dense adhesions     | 60 minutes                | Myocardial failure from delay                  |
| 236            | 2 days                                  | 34 days                                 | Cholecystitis; cystic duct obstructed      | 35 minutes                | Age, seventy-six years; delay                  |

# EARLY OPERATIONS ACUTE CHOLECYSTITIS

## RELATION OF POOR WOUND HEALING TO LENGTH OF ILLNESS

| No. | <i>At home<br/>before<br/>operation</i> | <i>In hospital<br/>before<br/>operation</i> | <i>Condition of wound</i> |
|-----|---|---|---------------------------|
| 68  | 2 days                                  | 2½ days                                     | Infection and separation  |
| 75  | 10 hours                                | 17 days                                     | Spontaneous rupture       |
| 76  | 5 days                                  | 11 days                                     | Non-union                 |
| 124 | 3 days                                  | 14 days                                     | Spontaneous rupture       |
| 153 | 4 days                                  | 1½ hours                                    | Spontaneous rupture       |
| 188 | 2 days                                  | 12 hours                                    | Spontaneous rupture       |
| 54  | 3 days                                  | 19 days                                     | Infection                 |
| 115 | 3 days                                  | 12 hours                                    | Infection                 |
| 179 | 4 days                                  | 17 hours                                    | Infection                 |

Delay before operation seems to be a contributing factor in post-operative spontaneous wound rupture but has little relation to wound infection.

## FOLLOW-UP

In Group A only three were noted. All satisfactory.

In Group B fifty-one were noted. Of these four had a hernia in the wound. Two had weak wounds. No follow-up was noted on one infected wound or on three of the ruptured wound cases. In this study no special effort was made to get a complete follow-up. The regular hospital records were used.

In Group B the oldest patient was seventy-six years. Died. Was sick fifty-four hours outside the hospital and thirty-four days in the hospital before operation. An effort was made to avoid operation. The youngest patient was thirteen years. Recovered. Had a large distended gall-bladder. The longest time in the hospital was seventy-nine days. Was sick four days before entrance. Waited seventeen days in the hospital before operation. Had pneumonia. One patient had had typhoid and ten pregnancies. Was entitled to gall-stones. One patient had been pregnant eighteen times.

## SUMMARY

This series of cases points definitely to the following conclusions:

### *First Series—Early Operation:*

1. There were no deaths from early operation when acute cholecystitis was the only disease present at the time of operation.
2. The necessary operations were simple ones.
3. The post-operative complications were few.
4. The days spent in the hospital were few.
5. The dressings were few.
6. There were no ruptured wounds.
7. The cost to the patient was low.

### *Second Series—Delayed Operation:*

1. The mortality was increased. Many of the deaths could be attributed directly to the delay.
2. Longer and more difficult operations were necessary.
3. The number of post-operative complications was largely increased.
4. The days spent in the hospital were much increased.
5. The dressings were much more numerous.
6. Ruptured wounds and post-operative ventral hernia occurred.



## SURGICAL ASPECTS OF GALL-BLADDER DISEASE\*

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FROM THE SECOND DIVISION OF BELLEVUE HOSPITAL

IN 1882, Langenbuch removed the first gall-bladder in an attempt to cure chronic cholelithiasis. The rationale of the operation was little understood for years afterward but with empiricism in treatment leading the way, thousands of gall-bladders have since been drained or removed to the comfort and satisfaction of patient and surgeon alike. Passing through a long period when the diagnosis of biliary lithiasis was made only in the presence of jaundice, evolution and advance in concepts of the diagnosis and treatment of biliary diseases have been due largely to the empiric type of treatment originally undertaken and to the carefully weighed conclusions drawn therefrom. These conclusions have been based on a mass of clinical data and operating-room interpretations in which bacteriologist and pathologist have given great aid until certain relatively clean-cut pictures of biliary lithiasis of bladder, ducts and radicals have been delineated. Inflammatory lesions of gall-bladder and ducts without lithiasis also became a matter of general recognition and gradually, associated lesions of liver, pancreas, appendix, stomach and duodenum or even more distant possible sources of infection have become attached to the picture until at present any conception of biliary disease must be broad in scope and adaptable in comprehension and take into consideration hepatitis, cholangitis, pancreatitis and cholecystitis as possible elements in the same picture in which lithiasis may or may not be found. True causation and the various factors concerned in these conditions of lithiasis and inflammation are still too little understood but the advances made in the treatment of the conditions in spite of this lack of knowledge must remain as one of surgery's great contributions and merits high tribute to the pioneers and their able followers in this branch of surgery. Elucidation of causes and relations of the various conditions remains a problem for clinician and experimental worker alike and will point the way to preventive treatment, better choice in surgical procedure and better after-care for the patient.

Embryologically liver, ducts, duodenum, pancreas and gall-bladder arise from the same nest of cells. The gall-bladder develops as a small solid bud on the side of the common duct, becomes hollow and enlarges and then becomes a diverticulum of the excretory duct of the liver. Its congenital absence in man is rarely noted. It is present in carnivora where food is taken at long intervals; it is absent in many herbivorous mammals such as the horse, the ass, the deer, the rhinoceros and the elephant. Yet biliary duct

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stones with cholangitis have been reported in autopsies on the horse and stones themselves in the elephant. Anatomically the human gall-bladder is a matter of record, grossly and histologically. In appearance it is thin-walled, translucent, bluish-white, compressible as to contents and in its normal state always contains bile. It is fairly vascular and its wall bleeds when cut. Variations from the above determine pathological changes, the extent of which may be very gross and easily recognizable, or minute, early and microscopic. That such latter changes may not be grossly recognized is obvious. Similarly that complete resolution may occur in such an organ by removal of the cause seems reasonable. In addition to the above, however, certain important anatomical features are present. A rich lymphatic network occurs in the wall of the gall-bladder which communicates freely with the periportal lymphatics about the common and hepatic ducts. Lymph nodes are found about the cystic, hepatic and common duct and their enlargement may be the criterion by which mild grades of cholecystitis are judged. These facts are mentioned as important at this time because they help to bear out the present-day theories as to the pathogenesis of cholecystitis without stones. For a long time it has been recognized that the pathway of infection of the gall-bladder must be either biliary, descending from the liver or ascending from the duodenum, hæmatogenous or lymphogenous. Each has its advocates with beliefs based on experimental data. While cholecystitis can be produced by bacteria in the bile, it would seem that the added element of foreign body (stone) or circulatory disturbance or stasis must always be present. On the other hand, a large amount of careful experimentation has been done in which bacterial injections into the portal vein have produced cholecystitis comparable to that in man. Moreover the lesion produced has been accompanied by the hepatitis and choledochitis which frequently accompany the lesion in man. Reasoning from these experiments, Graham holds that the portal infection produces a hepatitis which usually begins and is most marked in the interlobular or periportal tissues. A pericholangitis then occurs and because of the intimate anastomosis between the lymphatics of the intra- and extrahepatic biliary systems, a direct extension into the wall of the gall-bladder takes place, as well as into the common duct. He feels further that these ideas explain more reasonably than any others the associations of biliary tract infection with other lesions of the portal system such as appendicitis, duodenal ulcers, typhoid fever, etc. Certainly such an idea would also help to explain the preponderance of positive bacterial cultures from the macerated bladder wall as compared with the contained bile or stones and also those rarer cultures where the organisms grown from vesical wall and contents are entirely different. Whether this same lymphatic system can be followed down to the pancreas and will account for that "pancreatic lymphangitis" which Deaver and Sweet have described is still in question. It might be the happy explanation of the cause of continued pain or of the mild little colicky attacks seen in some of the cases of cholecystectomy for non-calculous cholecystitis as suggested by Judd where reopera-

tion has found no stones and drainage of the common duct has been a relieving measure. Archibald and other workers on pancreatitis might take exception to any such explanation.

The physiological function of the gall-bladder is still a point of controversy. That it fills during fasting and empties during digestion seems generally conceded. That it concentrates bile is also conceded. That it acts as a regulatory mechanism on pressure within the biliary duct system or that it empties by virtue of a contrary innervation between it and the sphincter of Oddi is not conceded. Even the presence of the latter as an entity is questioned. Cholesterol metabolism is associated with the gall-bladder but the rôle of the latter in it is undetermined. For this reason the exact status of the "strawberry gall-bladder" is in doubt. Experimentally it has been proved that the presence of the gall-bladder delays for twenty-four to forty-eight hours the appearance of jaundice when the common duct is completely blocked by ligation. Time precludes the mention of many other interesting observations on gall-bladder and ducts made recently, particularly since the introduction of the phenolhalogen dyes has enabled closer study. Liver function is closely associated with the entire problem. Solution of this problem will probably come from further work along these lines by both physiologist and experimental surgeon.

Thus far little mention has been made in this paper of gall-stones as such. Their occurrence has been recognized for hundreds of years, chiefly in the gall-bladder and the main ducts. Too little attention has been paid to the possibilities of their genesis in the smaller ducts and radicals of the liver itself. A recognition of this latter fact and a knowledge of the factors concerned in the rapid formation of gall-stones may point the way to better treatment of that small percentage of cases where cholecystectomy and even common-duct drainage do not completely answer the problem. Digby has recently commented upon the frequency of intrahepatic stone formation among the Hong Kong Chinese as contrasted with its rarity among Europeans. In the past year at Bellevue we have had two such cases. One young lady of twenty-four had a simple cholecystectomy and healed well. On the day on which she was to be discharged, a slight icteric tint was noted and she was kept in the hospital. Increasing jaundice with apathy and lack of appetite led to a second exploration at which time no obstruction of the common duct by previous injury or stone was found but within it were two small stones and from the right hepatic duct were also removed several small cholesterol stones. None was reached in the left hepatic duct where we also assumed their presence. The liver was small and dark. The pancreas was so soft to palpation that it could not be recognized as pancreatic tissue. Death resulted in this case but the genesis of the hepatic and probably intrahepatic duct calculi and their relationship to the previous cholecystectomy give much food for thought. Similarly a white man of thirty-seven years of age, was admitted with the history of having had a cholecystostomy performed nine years ago. We were unable to learn whether or not his

## SURGICAL ASPECTS GALL-BLADDER DISEASE

gall-bladder contained calculi at that time. He was free from symptoms until last summer when, after two months of sharp symptoms, his gall-bladder was removed. It was a difficult cholecystectomy for chronic inflammation without calculi. He was fairly well for two months, following which he was readmitted to the hospital with jaundice and recurrence of symptoms. His common duct was explored and many stones removed. With drainage he continued to discharge stones intermittently throughout the fall, some small, some fairly large, many in general appearance corresponding to the configuration of small segments of branching bile ducts. In this case too, death resulted, but cholecystectomy apparently induced changes in the physical or chemical conditions of his biliary system which made him a small factory for gall-stones. He passed more stones than any combination of common and hepatic ducts could possibly account for. These cases are mentioned as illustrative of unsolved problems which confront us. They are hardly to be accounted for on the basis of overlooked calculi, although every surgeon acknowledges this possibility in any given case.

For the purpose of this paper there have been briefly reviewed 333 cases of biliary tract disease which have been operated upon on the Second Surgical Division of Bellevue during the past few years. Certain facts and conclusions will be presented. The incidence of the disease as to sex shows about two and one-half females to one male; as to age 58 patients between twenty-nine and thirty, 106 between thirty and forty, 81 between forty and fifty, 88 between fifty and sixty. The anthropologic type of the patient remains the same as ever although it seems that recently more patients not quite so fat and of younger years were now seeking treatment. The duration of the disease itself has varied in the history of the patient from one day to fifteen years.

Diagnosis of the pathological condition present has placed its main dependence on the well-elicited history plus the physical examination. The value of the various laboratory and röntgenological aids is in no way minimized by this statement but the main reliance in diagnosis will remain the good clinical history and examination. The icteric index is more exact than the eye in its measure of increase or decrease in jaundice. The Vandenberg reaction may separate obstructive and hæmolytic or toxic types of jaundice but will not localize the obstruction. The phenolhalogen dyes in the cholecystogram will corroborate diagnoses and differentiate in many cases of doubt. We have found them in this way very useful but in no sense a substitute for clinical diagnosis.

Cholecystography represents a means of diagnosis and of refinement in diagnosis which is of the utmost value but its use in a large hospital must be carefully checked as to the preparation of the patient, the retention of the dye when taken by mouth and the careful timing between visualization of the gall-bladder and its emptying under the stimulus of fat ingestion. Interpretation will be largely in the hands of the skilled röntgenologist. Its greatest value in our experience has been first, failure to visualize the gall-bladder

at all under a carefully supervised technic, and second, the positive visualization of stones, and abnormalities with slow emptying time. Our experience with liver function tests, except as associated with cholecystography, has been nil but we foresee difficulties in the practical application of any functional test to an organ with so tremendous a margin of safety as the liver.

In our series, five cases of perforated gall-bladder have been met, three with spreading peritonitis, two with local peritoneal abscess. These were all apparently due to stone although no stones could be found in one. Her condition did not warrant a search. Three died. Acute suppurative or necrotic and gangrenous gall-bladders have been met thirty-eight times, a much higher incidence than in most series of cases. Diagnosis and classifications here have been based upon gross pathological and microscopic pathological evidence. Non-calculous cholecystitis has been met fifty-four times. The balance of the cases have been calculous cases with varying degrees of cholecystitis, or those more unfortunate ones with common duct stones.

Upon these cases of acute and chronic nature, 299 cholecystectomies have been performed. This has been combined with other surgical procedures such as appendectomy gastroenterostomy, repair of hernia, and so forth in a relatively small percentage of cases. The mortality for this group as a whole has been twenty-one or 6.3 per cent. Eliminating the acute and perforating lesions from the group would reduce this figure to about 4 per cent. The larger figure, however, gives, we believe, a better picture of the results on a general service in a metropolitan hospital in which the work is done by a fairly large group of men. It compares favorably with the statistics (7.2 per cent.) of Hitzrot and Cornell in their review of 400 cholecystectomies at New York Hospital in 1926. Deaths due to myocarditis and acute cardiac failure, six; shock, three; pneumonia, five; peritonitis, three; overlooked stone in ampulla of Vater, one; cholæmia, two; and cause not given, one. Cholecystostomy has been done twenty times with a mortality of six. It is obvious from these statistics that cholecystostomy has been reserved for the very sick individual or those in whom the local conditions made it seem clearly advisable. Without going into the relative merits of these two operations, it would seem that each has its distinct place in gall-bladder surgery and the wise surgeon will frequently choose a drainage operation or a cholecystectomy through the ampulla in order to conserve the strength and best interests of his patient. Nothing but sound judgment based on large experience can meet the individual indications for such a choice between two procedures.

Operation for common-duct calculus has in this series been an operation with high mortality (over 20 per cent. in twenty-six cases). Done in the type of patient who presents indications, with or without cholangitis, with or without cholecystectomy, its outcome is difficult to prophesy. Of late there has been a growing feeling on our service that in such instances the very least possible amount of operative interference should be added to the necessary common-duct exploration. By this is meant the simplest type

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of cholecystostomy and that cholecystectomy should be reserved for a later date. While this small number of cases is valueless for conclusions, nevertheless they emphasize the importance of the early removal of calculi from the biliary tract before common-duct obstruction occurs. They also serve to emphasize the importance of a clearer understanding of the nature of that terminal condition now called cholæmia. The German surgeon Kehr in a review of a large number of cholecystectomies once made the astounding statement that he found stones in the common duct in 20 per cent. of his cases in which there was not the slightest sign of their presence, neither jaundice nor intermittent fever. While palpation of the common duct has been the routine in all of our cholecystectomies, no such incidence of common duct calculi has been found.

In surgical technic, practically all of the gall-bladders in the above series have been removed from the fundus downward, leaving the peritoneal flap wherever possible. We feel that this method, in ease and safety of procedure, has more than justified itself, although we recognize the theoretical advantages of removal from duct outward. All cases have been drained by either a cigarette drain to Morrison's pouch or more frequently combining this with one to the stump of the cystic duct. Drainage of this type presents no disadvantages, we believe, and is an added factor of safety in case of bile leakage which we find to be the rule, or in case of infection which is a potential factor in every case of gall-bladder removal. It makes for the safety of the patient and the peace of mind of the operator.

In the follow-up, sixteen post-operative ventral hernias are noted—an incidence of less than 5 per cent. Probably others have been seen by other surgeons which might make this figure higher. It would seem that about three months must elapse after operation that we might call a period of readjustment when the patient requires some dietetic supervision and bowel regulation. Following this is the period in which final results may be evaluated. We expect an excellent result, *i.e.*, freedom from symptoms in approximately 80 per cent. of our cases of cholelithiasis. In non-calculous cases these results are not so good. Many of them continue to complain of symptoms of qualitative indigestion, gas and feelings of distention that were present before operation. What determines the apparently better result in the calculous cases is still a mystery. Comfort and a sense of well-being are relative terms. Perhaps the calculous cases show the effects of the removal of both a mechanical and inflammatory irritant, whereas the non-calculous cases have shown purely an inflammatory irritant. Certainly the associated lesions are as frequent or more frequent in the stone cases than in the non-stone cases.

## RECONSTRUCTION OF THE COMMON BILE DUCT BY END-TO-END ANASTOMOSIS

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THE disadvantages encountered in the use of the ordinary rubber catheter, the rubber T-tube, and the "buried" drainage tube in drainage and reconstructive operations upon the common and hepatic bile ducts, led me to devise an L-shaped rubber catheter. This L-shaped rubber drainage tube was used in the three following cases. The results were entirely successful and are of sufficient interest, I believe, to justify their being reported.

CASE I.—A woman, aged forty years, was seen in consultation with Dr. Milton H. Prosperi April 14, 1925, at the Providence Hospital, Washington, D. C. She was badly jaundiced, nauseated and vomiting. Temperature 100°. She stated that for six years she had had dyspepsia and that since November, 1924, she had had attacks of pain in her upper abdomen after each meal, lasting from one-half hour to two hours. Accompanying the pain there had been gas and bloating of the abdomen. The pain sometimes extended from the epigastrium to the back and upward under the right shoulder-blade. She had had nausea and vomiting at intervals for several years. A few weeks before she presented herself for examination the attacks of pain had become frequent and the jaundice had gradually deepened. Slight attacks of chills, fever, nausea, and vomiting accompanied the jaundice. The stools had become clay-colored.

At operation May 15, 1925, we found a very firm, œdematous liver, an inflamed gall-bladder, an enlarged and thickened common bile duct, and an inflamed pancreas. The gall-bladder, which contained one stone, was removed. As the cystic duct was opened there escaped from it a large amount of "white bile." The common bile duct was incised and explored with a probe. A large stone was felt at the ampulla of Vater. After considerable difficulty it was dislodged by means of a stone forceps. As the stone was being delivered through the choledochotomy the friable duct was split transversely and almost divided. In order to repair the damage to the common bile duct it was necessary to make an end-to-end anastomosis. An L-shaped catheter was passed downward through the stump of the cystic duct into the common bile duct. Over the portion of the catheter which lay in the common bile duct a reconstruction was effected by an end-to-end anastomosis made with interrupted chromic catgut sutures. The bell end of the catheter was brought out through the abdominal incision. About twenty-four hours after the operation bile started to flow through the catheter and there was considerable external drainage. On May 18 the external flow of bile ceased and on May 19 bile appeared in the stool. On May 25 the tube was clamped. After four days bile was appearing in the stool and there was no sign of obstruction. On May 29 the L-shaped drainage tube was removed. Since the operation this patient has been kept under observation and there has been no evidence of biliary obstruction.

CASE II.—A man, aged sixty-one years, entered Garfield Hospital, Washington, D. C., August 17, 1925. He was slightly jaundiced and had pain and soreness in the upper abdomen. Temperature 102°, leucocytes 15,800. There had been no previous history of jaundice or of clay-colored stools, but he had been subject to indigestion off and on for twenty years. On August 2 he had had a sudden, severe pain in the upper abdomen. It did not radiate. He induced vomiting which gave him relief. He had had no further trouble until August 12 when he had another attack of pain across

## RECONSTRUCTION OF COMMON BILE DUCTS

the upper abdomen. The pain continued at intervals but there were no chills. An examination of the abdomen revealed an enlarged liver with a globular mass extending downward, which was thought to be the gall-bladder.

At operation August 20, 1925, a small oblique incision was made in the upper right quadrant of the abdomen about 2 inches below the costal border. The gall-bladder was found to be greatly distended and acutely inflamed. Its thickened, purulent contents were emptied through a trocar. The trocar opening was dilated and several small stones were removed from the gall-bladder. A stone which was found to be impacted in the cystic duct was removed. The gall-bladder was drained. Following the operation the patient made a very satisfactory recovery with the exception that he had an external biliary fistula.

November 10, 1925, a second operation was performed to close the biliary fistula. The gall-bladder was found to be considerably inflamed and the adjacent structures were firmly adherent to it. The common bile duct was patulous but there was much inflammatory induration which partially obstructed it. The gall-bladder was removed, the common bile duct was opened, and a rubber T-tube was inserted for drainage. Following the operation bile appeared in the stool, and it also drained externally through the stem of the T-tube. November 28 the rubber T-tube was removed. Following its removal there was some external drainage but the stools contained bile. The patient was well enough to leave the hospital on December 2, 1925. For about a month he was in good condition. He then began having discomfort in his upper abdomen and a loss of appetite. About this time he noted that he was getting jaundiced and that the stools were getting lighter in color. When he was examined February 13, 1926, he was deeply jaundiced. He had lost weight and was very weak.

At operation February 20, 1926, a stricture of the common bile duct was found at the site at which the duct had been opened and the T-tube placed at the second operation. The stricture completely obstructed the duct. A resection of the duct was made to excise the stricture. The continuity of the duct was then reestablished by an end-to-end anastomosis over an L-shaped rubber drainage tube. To accomplish this a slit was cut in the inferior portion of the common bile duct, the tip of the L-shaped rubber catheter was passed into the lumen of the duct, and the divided ends of the bile duct were drawn together over the catheter with interrupted chromic catgut sutures. Following this operation the patient had profuse external drainage of bile through the tube for several days. Then bile appeared in the stool and the external drainage gradually diminished. The L-shaped rubber tube was allowed to remain in place for six weeks when it was removed without difficulty. Following the removal of the catheter, there was profuse drainage of bile for several days. The patient was well enough to be dismissed from the hospital on April 10, 1926. He has been under observation and has been seen many times since his last operation. There has been no jaundice and no return of symptoms that would indicate a recurrence of the stricture of the common bile duct.

CASE III.—A man, aged forty-two years, was seen in consultation with Doctors Clark, Perry, and King August 13, 1927, at the Emergency Hospital, Washington, D. C. The patient was jaundiced and undernourished. He stated that about three years previously he had had considerable gaseous indigestion with pressure and soreness in the epigastrium. Attacks of pain occurred frequently and on several occasions they were severe enough to require a hypodermic injection of morphine. He became badly jaundiced and was told that he had a blocking of the bile duct. He also stated that his gall-bladder had been removed in October, 1925. Following the cholecystectomy he was fairly well for about a year, and then had a return of indigestion similar to that which he had experienced before the operation. In May, 1927, he had an attack of severe cramping pain in the epigastrium which was followed by a slight chill and the following day by jaundice. The jaundice lasted three or four weeks. The soreness in the epigastrium was more or less continuous. The jaundice gradually returned until



at the time of our examination it was quite deep. Chills and fever accompanied the jaundice.

At operation August 15, 1927, it was found that the gall-bladder had been removed. The stump of the cystic duct was identified. One-half an inch above the stump of the cystic duct there was a stricture of the hepatic duct. Both the common and hepatic ducts were enlarged and their walls thickened. Stones could be palpated above and below the stricture. The common bile duct was incised and an attempt was made to pass a probe upward. As the smallest probe could not be passed through the stricture, the stricture was incised longitudinally. This gave access to both portions of the bile duct. The stones were removed from the inferior portion. With a probe the ampulla of Vater was dilated. Then a uterine dressing forceps was passed through the ampulla and opened to further dilate it. The stones in the hepatic duct and in the liver ducts were removed with stone forceps. The stricture was excised by resection. A small slit was made in the hepatic duct just below its bifurcation. Into this opening an L-shaped catheter was introduced with its tip pointing downward toward the pancreas. Over the L-shaped catheter an end-to-end anastomosis was made with interrupted sutures. The bell end of the catheter was brought out through the upper end of the abdominal incision. Following the operation there was a small amount of external drainage of bile through the catheter. In a few days bile appeared in the stools. The jaundice gradually faded. The L-shaped catheter was removed in about two weeks. The wound healed and the patient was discharged on the twenty-fifth day. The patient has been under observation for the three years since the operation. He was last seen on September 6, 1930. There has been no return of jaundice or of symptoms indicative of biliary obstruction.

The L-shaped rubber drainage tube maintains the lumen of a bile duct at the site of anastomosis; it provides and insures a means of adequate internal and external drainage of bile; and it prevents a contraction of the circular scar after the healing of the anastomosis. It can be inserted into either the superior or inferior portion of a bile duct through a small slit in the duct wall; it can be held securely in position; and yet it can be removed at the time desired without injuring the bile duct or tearing the anastomosis. The short section of the L-shaped tube which lies within the bile duct extends from its point of entrance in one portion of the duct, upward or downward as the case may be, across the anastomosis into the other portion of the duct, thereby maintaining the lumen of the duct at the annulus of the anastomosis. It is desirable that the lumen of the duct be maintained by a rubber drainage tube in order to prevent an obstruction which might otherwise result from oedema of the inverted edges of the mucous membrane at the suture line. In the short section of the L-shaped tube which lies within the duct, there are six openings, one in the tip, one in the bend of the elbow, and four placed laterally. These openings secure through-and-through drainage from one portion of the duct to the other, thereby providing a means of adequate internal drainage of bile. The openings also secure a means of adequate external drainage through the long section of the tube which passes through the slit in the duct and out through the abdominal wall. External drainage is desirable in case the inferior portion of the common bile duct becomes obstructed and does not convey the bile into the alimentary canal. The portion of the L-shaped rubber drainage tube lying within the lumen of

# RECONSTRUCTION OF COMMON BILE DUCTS

the bile duct supports the anastomosis during the process of healing and later prevents contraction of the circular scar which forms in the suture line.

After the short section of the tube is inserted into the lumen of the bile duct through a small slit made in its wall, one or two chromic catgut stitches

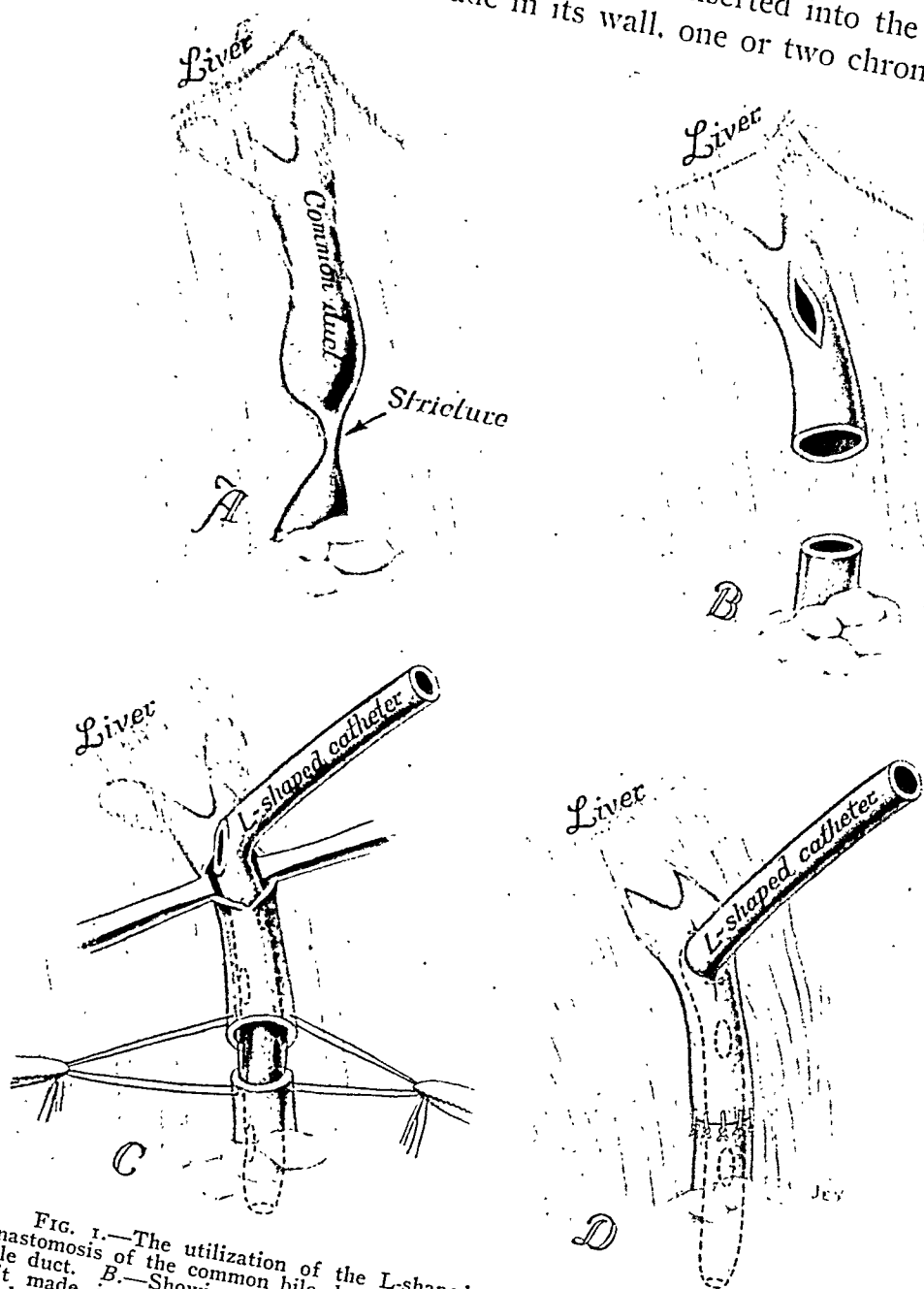


FIG. 1.—The utilization of the L-shaped rubber catheter in an end-to-end anastomosis of the common bile duct. *A*.—Showing a stricture of the common bile duct. *B*.—Showing the stricture excised by a resection of the duct and a slit made in the superior portion of the duct for the introduction of the L-shaped catheter. *C*.—Showing two posterior and two lateral sutures in place and the L-shaped catheter being introduced into the duct. *D*.—Showing the anastomosis completed over the L-shaped catheter.

are then used to close the opening snugly about the tube. The long section of the tube is brought out through the abdominal incision. The tube is held in position at first by a silkworm suture placed in the skin and fascia and wrapped about the stem of the tube; and after the wound has healed, by strips of adhesive plaster attached to the stem of the tube and to the surface

of the skin. The tube can be withdrawn easily at any desired time without the slightest injury to the anastomosis. The small slit in the wall of the duct through which the tube passed heals perfectly.

The technic employed in utilizing the L-shaped rubber drainage tube in an end-to-end anastomosis varies slightly depending on whether the operation is a primary one in which a division or injury of the bile duct has been recognized, or in which a benign or a congenital stricture has been resected; or whether it is a secondary operation in which reconstruction is necessary as a result of a previously unrecognized division or injury of the duct, or of a post-operative stricture. In one of the latter conditions it is necessary to search for the duct ends or for the place where the duct has been obliterated. If the bile duct is found to be obstructed by a stricture, the stricture can be removed by resection, although if too large a segment of the duct has to be excised an end-to-end anastomosis should not be attempted. If the duct is found to be divided and the gap is not too great, the ends will have to be mobilized and prepared for anastomosis.

With two free ends that can be approximated, either at a primary or secondary operation, a longitudinal incision should be made in either the superior or inferior portion of the bile duct through which to insert the L-shaped rubber drainage tube. Two sutures are passed posteriorly through the walls of the duct ends and two are passed laterally. The ends of these sutures are not tied but are held in artery forceps. The fenestrated portion of the L-shaped tube is then inserted through the slit in the duct wall into the lumen of one portion of the duct, across the intervening space, into the lumen of the other portion. The anastomosis of the duct is finished off by approximating the cut ends. This is accomplished by tying the posterior and lateral sutures, and by placing and tying two additional lateral sutures and two anterior ones (Fig. 1).

*Conclusions.*—The L-shaped rubber drainage tube gave satisfactory results in the three cases reported because:

1. It supplied a means of adequate internal and external drainage of bile.
2. It lent itself to secure and firm anchorage in the bile duct and in the abdominal wound.
3. It was easily removed at the time desired without damaging the anastomosis.

# PARTIAL AND SUBTOTAL GASTRIC EXCLUSION \*

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IN JANUARY, 1930, when operating on a patient for an hour-glass contraction of the stomach, the procedure of partial gastric exclusion described herein and previously reported by Devine in 1925 and again in 1928 was resorted to. The object of this paper is to portray the findings in the above-mentioned patient and to report the results of a series of experiments on dogs in which from one-half to four-fifths of the stomach was excluded followed by a Polya anastomosis.

**CASE.**—The patient was a female fifty-two years of age whose chief complaint was stomach trouble of twenty years' duration, consisting of periodic attacks over several months and characterized by pain usually coming on two hours after meals, belching of gas, sour eructations and vomiting, the vomitus being free from blood. For several weeks prior to operation her pain at night was severe and more or less continuous. There was loss of thirty-two pounds in weight. The patient was undernourished. The abdomen was flat and soft. Neither viscera nor masses were palpable. There was tenderness, extremely slight and only on deep palpation, high in the epigastrium. This was interpreted as relatively normal. The urine contained a faint trace of albumin and a moderate number of white blood cells. Hæmoglobin was 80 per cent., red blood cells 4,200,000, white blood cells 7,000, polymorphonuclears 70, lymphocytes 30.

**X-ray Report.**—The skiagraph (Fig. 1) reveals the presence of an organic hour-glass due to an ulcer of the lesser curvature pars-media. At six hours there is a small gastric retention in the lower locule. The duodenum was negative. These findings indicated a gastric ulcer with organic hour-glass.

**Operation.**—January 22, 1930. Gas-oxygen-ether anæsthesia. Revealed 1. Typical hour-glass contraction in pars-media. 2. Extensive crater ulceration on lesser curvature and posterior wall which was fixed. The stomach was divided between Payr's clamps after ligation of left gastric and gastro-epiploic arteries. The distal cut end was then closed with a through-and-through lock stitch and inverted with a sero-muscular suture. The jejunum was then brought through an opening in the transverse meso-colon and a typical Polya anastomosis made with the open end of stomach. The abdomen was closed in layers without drainage.

**Course.**—Within twenty-four hours vomited four times small amounts of dark bloody fluid and vomited twice on the third post-operative day. Temperature rose to 101° degrees on the second day and was normal on the fifth. Sutures were removed on the eighth day and wound was clean. Patient discharged from hospital on the fourteenth day.

With the exception of a vomiting attack six weeks after operation following an overloaded stomach the patient has been symptom-free and has gained twenty pounds in ten months. An X-ray (Figs. 2, 3, 4) examination at this time reveals a well-functioning small stomach entirely to the left of the mid-line. At six hours the barium meal has passed into lower ileum and cæcum. Gastric analysis on Jan. 28, 1931 reveals no free hydrochloric acid and a total acid of 5.

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\* Read before the New York Surgical Society, January 28, 1931.



FIG. 1.—Reproduction of roentgenogram with barium meal showing hour-glass constriction. Arrow indicating ulcer.

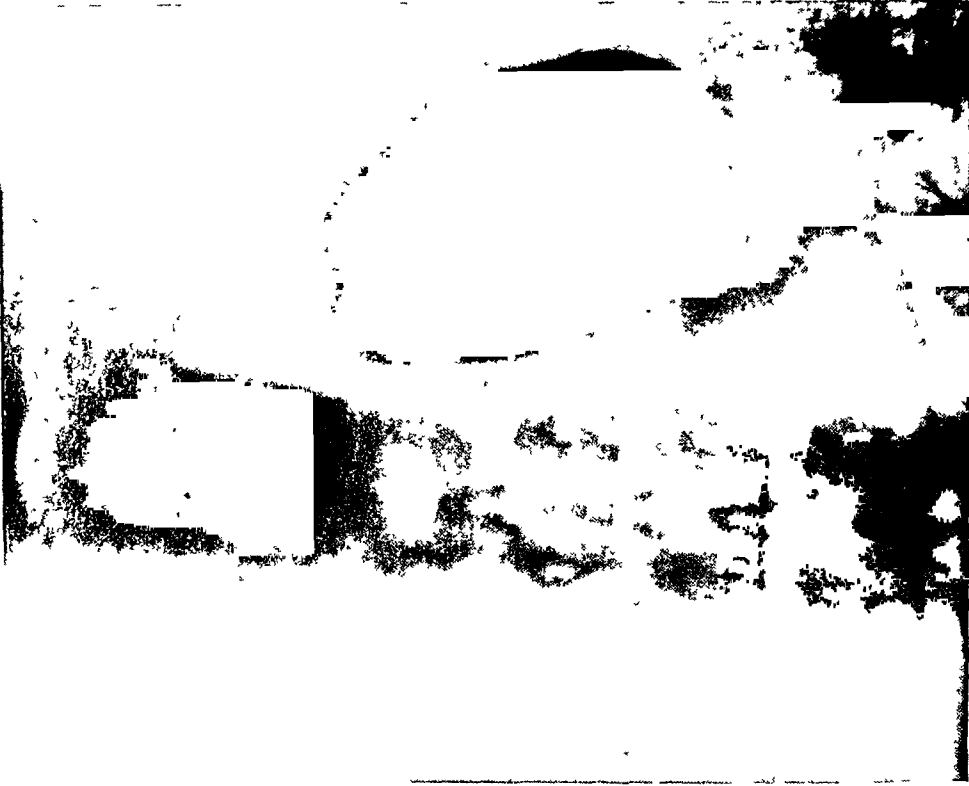


FIG. 2.—Reproduction of roentgenogram with barium meal ten months after operation.

# PARTIAL AND SUBTOTAL GASTRIC EXCLUSION

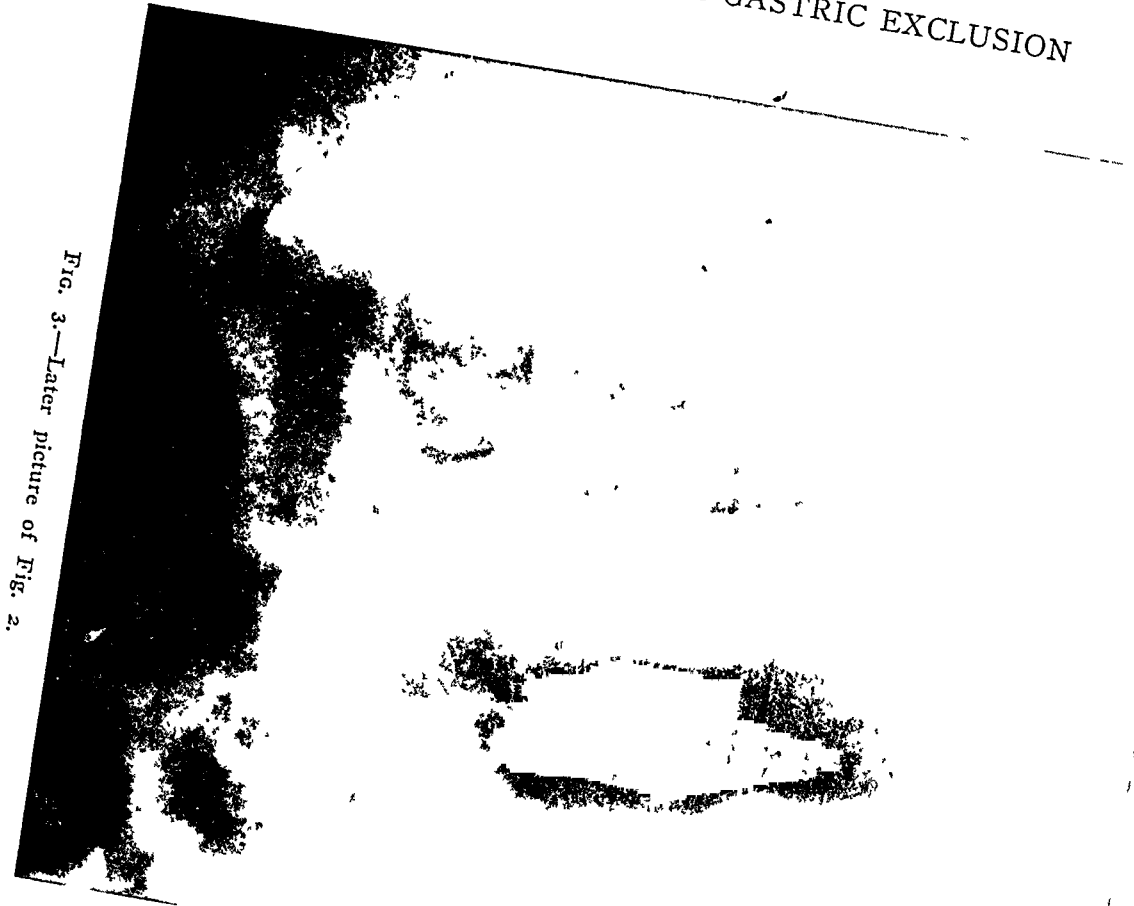


Fig. 3.—Later picture of Fig. 2.



Fig. 4.—Six hour picture, showing gas bubble in stomach (arrow). Barium in terminal ileum and cecum. Cont.

## ANIMAL EXPERIMENTS

Exclusion operations were performed on twelve dogs. Five of the dogs died, three from distemper, one from a peritoneal abscess and one from shock. In the latter dog in order to remove enough of the stomach it was

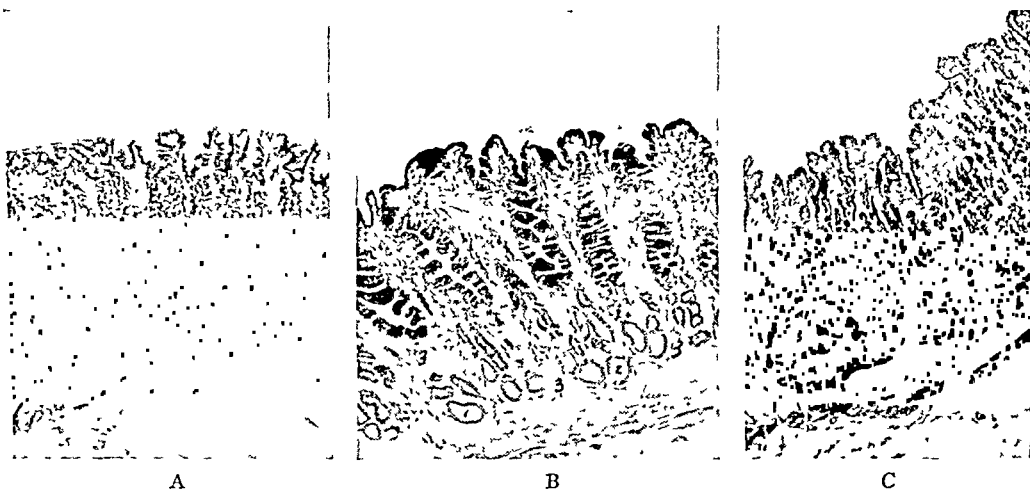


FIG. 5.—Low power. A—Control removed at time of operation. Acini closely packed with cells. Parietal cells deeply staining. B—Section from excluded area after fourteen days. 1 and 2—dilated acini. 3—Increase in inter-glandular stroma. No parietal cells. C—Section from stomach at autopsy. Acini and cells resemble those in A.

necessary to remove the spleen. In these five dogs the tissue was not fit for microscopic section. A gross and microscopic study was made in the other seven dogs.

It was found that the most satisfactory fixative was Bouin's solution and

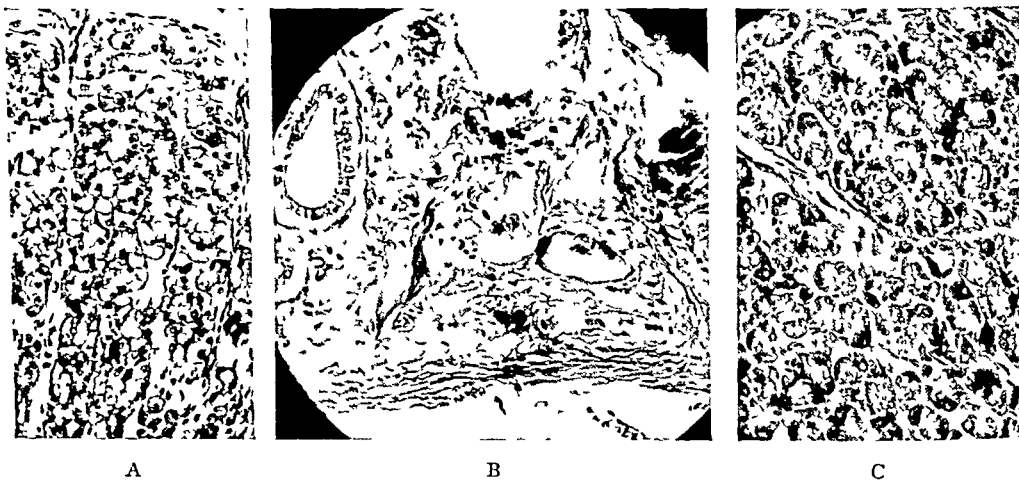


FIG 6—High power. B—Showing glandular degeneration and increase in stroma.

the most satisfactory stain Trichromique was phosphomolybdique differentiation as described in Masson's "Pathology," pages 688-690.

The operation on dogs is similar to that performed on humans and as already detailed in the case report. From one-half to four-fifths of the stomach was excluded. The excluded portion after suture immediately con-

## PARTIAL AND SUBTOTAL GASTRIC EXCLUSION

tracted into a tube and retracted posteriorly to the lower portion of the duodenum. Contraction took place in such a manner that the suture line which was made in a sagittal plane lay horizontal and in the position of the lesser curvature. These contractions are further described in the protocols.

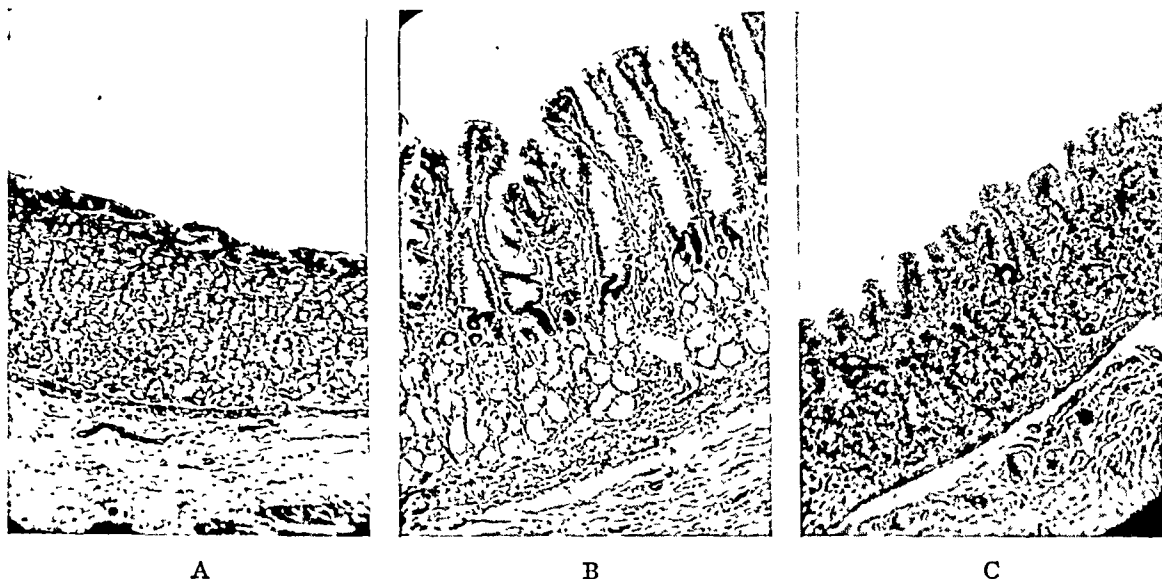


FIG. 7.—Low power. A—Section from stomach to be excluded. C—Section from functioning stomach at autopsy. B—Section from excluded area at one month and twelve days, showing further advanced degeneration.

Devine has advised on oblique section of the stomach to include more of the fundus, stating also that this gives a better tube effect in the excluded portion. From this standpoint, however, such section is not necessary.

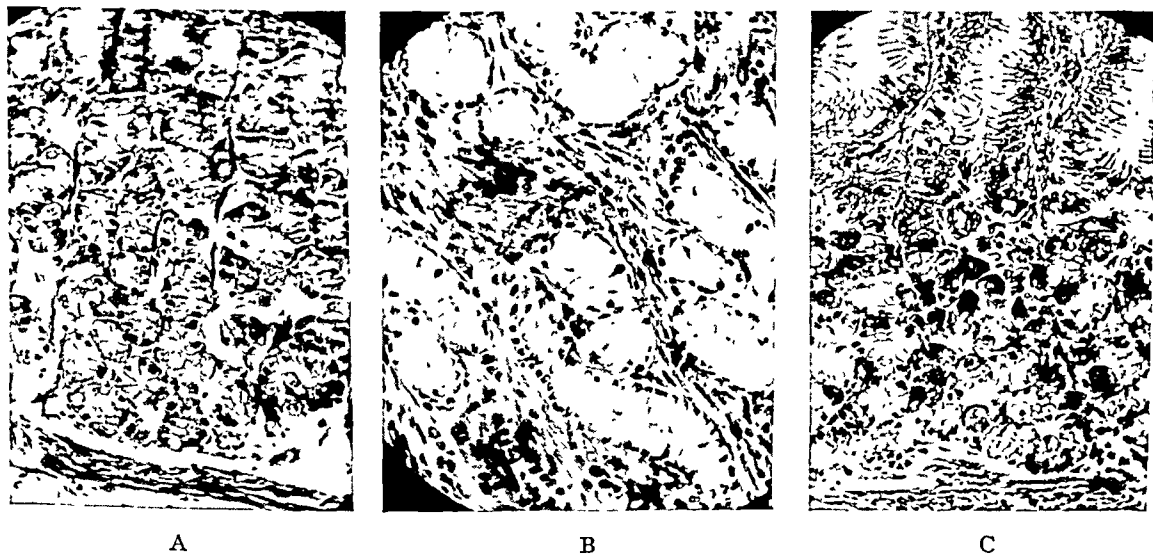


FIG. 8.—High power. B—Note distortion and disappearance of nuclei also fibrosis.

### HISTOLOGIC STUDY

The mucus-secreting or surface glands show no demonstrable change, except that they are thrown into deeper folds. Globules of mucus are invariably present in the cells in the excluded area. From the twelfth day on, the digestive glands are in a resting phase. This is shown by dilation of acini with large lumina. There is absence of granules in the chief and parietal cells. The nuclei of these cells are contracted,



distorted or degenerated. In some areas, the entire acinus is degenerated and represented by débris. The parietal cells in general seem to undergo more rapid dissolution than the chief cells, as may be seen in the accompanying chart. They were absent after the twelfth day except in one instance when they were undergoing degeneration.

CHART OF PARIETAL CELLS

| Section from<br>area to be<br>excluded | No    | Section from<br>excluded<br>area | Time              |
|--|-------|----------------------------------|-------------------|
|  | 11533 | Present                          | 6 days            |
|  | 11532 | Absent                           | 12 days           |
| Present in large numbers               | 11630 | Absent                           | 14 days           |
| Present                                | 11537 | Absent                           | 1 month           |
| Present in large numbers               | 11614 | Absent                           | 1 month, 12 days  |
| Present                                | 11586 | Degenerating                     | 1 month, 18 days  |
| Present                                | 11667 | Absent                           | 3 months, 10 days |



FIG 9—A—Oesophageal opening B—Jejunal opening C—Excluded portion of stomach



FIG 10—A—Oesophageal opening B—Jejunal opening C—Excluded portion of stomach D—Duodenum

The interglandular stroma is greatly increased in amount and areas of fibrotic replacement are apparent.

In the muscularis, microscopic changes are much less pronounced. At fourteen days there are signs of nuclear degeneration and complete lack of undulation in the muscle spindles. At one month and eighteen days, areas of complete degeneration and fibrous tissue replacement are manifest.

The following is a brief résumé of the microscopic findings in the excluded area:

Specimens for controls were taken from the area to be excluded and immediately fixed in Bouin's solution. The dog is a particularly good animal for these experiments for in no instance except in the excluded area was there a sign of a resting phase in the mucous membrane. All the tissues used for microscopic purposes were taken from dogs killed with ether, and were immediately placed in fixative so that autolysis could

## PARTIAL AND SUBTOTAL GASTRIC EXCLUSION

not take place. The time between operation and autopsy varied from six days to three months and ten days.

At six days: There is a questionable early degeneration of parietal cells, absence of granules in the chief cells and absence of mucus.

At twelve days: Resting phase of mucous membrane. Absence of parietal cells. Early degeneration of glands—absence of granules in cells with no mucus and no change in stroma.

At fourteen days: Resting phase of glands which are better preserved than at twelve days, but there is marked increase in stroma; a small amount of mucus is present. Parietal cells are not recognized. (Figs. 5 and 6.)

At thirty days: Advanced stage of glandular degeneration with marked increase in stroma and fibrous replacement. Parietal cells are absent. There is relatively little mucus present. (Figs. 7 and 8.)

At forty-two days: This is similar to preceding, with less connective tissue reaction and much more mucus in the surface glands. Parietal cells are absent.

At forty-eight days: Individual cells and glands are destroyed—numerous parietal cells are present but in various stages of disintegration. Stroma shows a patchy fibrous increase and mucus is present in the surface cells.

At three months and ten days: There is absence of parietal cells and glandular degeneration with increase in stroma and fibrous tissue replacement; relatively little mucus is seen in surface cells.

### SUMMARY

Devine<sup>1</sup> reported the treatment of thirty patients with old callous ulcers on the posterior wall of the duodenum by pyloric exclusion and Polya anastomosis with results which were excellent except in three instances. In one of the latter melæna occurred. In two others jejunal ulcers developed. He later operated on eight patients, increasing the area of exclusion with excellent results. In his second paper<sup>2</sup> he reports the same treatment of eighteen duodenal ulcers with one death and of an hour-glass stomach in which Billroth No. 2 was done, the patient remaining symptom-free twelve years later.

Our experience as surgeons is certainly small in this type of gastric surgery, but it seems fair to conclude that the exclusion operation is one which may be resorted to in complicated gastric ulcers, if not in others. The experimental evidence here offered is that the excluded portion immediately contracts and that the glands producing hydrochloric acid, the ever-present accompaniment of ulcer, undergo degeneration and are replaced by fibrous tissue.

### REFERENCES

- <sup>1</sup> Devine, H. B.: Basic Principles and Supreme Difficulties in Gastric Surgery. *Journal of Surgery, Gynecology and Obstetrics*, vol. xl, p. 1, 1928.
- <sup>2</sup> Devine, H. B.: Gastric Exclusion. *Journal of Surgery, Gynecology and Obstetrics*, vol. xlvii, p. 239, 1928.

## DUODENO-CUTANEOUS FISTULÆ

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THE etiology of a duodenal fistula is varied. From a review of the literature, from clinical observations and from a study of autopsy material, the following are some of the most frequent causes:

1. Perforated duodenal ulcer, untreated in the acute state, with subsequent localized abscess, and necrosis of the gut.
2. Difficult upper abdominal surgery where the duodenum has been devitalized, especially gall-bladder surgery, nephrectomy, or liver abscess.
3. Delayed healing following suture of the gut.
4. Faulty suture technic or faulty suture material.
5. A drain of any material adjacent to a suture line in the gut.
6. Unrecognized bullet wound in the retroperitoneal portion of the duodenum.
7. Periduodenal ulcerations.
8. Rupture of the fixed portion of the duodenum from a fall or blow on the abdomen.
9. Rupture of a diverticulum of the duodenum.

RAZZABONI,<sup>1</sup> whose reported case is quoted in this paper, did some experimental work on the etiology of duodenal fistula. The following is a summary of his work. He experimented on dogs, and produced in them lesions similar to those accidentally produced in upper abdominal surgery: (1) simple ligature of the duodenal vessels; (2) simple decortication of the wall of the duodenum; (3) ligature and decortication at the same time; (4) production of a periduodenitis by means of chemical agents (concentrated tincture of iodine) or of a very superficial decortication and some time later duodenolysis with or without ligature of the duodenal vessels; (5) duodenotomy and immediate scraping of the duodenum in one or several steps on normal duodenal walls either prior to or contemporaneously with ligature of the vessels or of decortication; (6) parietal ligature of the duodenum or temporary application (from one to three days) or a parietal forceps; (7) active cauterization of the duodenal walls; (8) application for a certain period of a permanent drain at the back of the duodenum.

The animals which were used for the experiments were kept on a strict diet and after death had occurred an accurate necroscopic examination was performed which was complemented by a thorough histological examination. The observations which he made in the fourteen cases have shown that application of a permanent drain seems to have a damaging effect and in a great many cases leads to the formation of a duodenal fistula. These experiments showed, even where a drainage tube was left in place for only a short period, that the results were constantly unfavorable. The objection which may be raised, that the ill results were probably due to secondary infarcts, is not substantiated on account of the precautions which were taken. These unfavorable results were caused by anatomico-biological factors which ordinarily have the task of repairing a process, but were hindered by the drainage itself. The mere presence of the drainage tube causes no damage as is proven by two cases where it was left in place from three

to four days at the duodenal surface and when removed, the wall of the duodenum was in perfect condition.

WALTERS and BALLMAN<sup>2</sup> have done an excellent piece of work on the chemistry of the blood in duodenal fistula. Their findings show lowered chlorides and increased urea in these patients. They also demonstrated a disturbance in the gastro-intestinal motility which developed coincidentally with the fistula. Various experimental operations were performed on dogs and their blood chemistry determined. They found (1) lowered chlorides and elevated urea in dogs where stomach, duodenal and pancreatic secretions were lost through the fistula. The dog was given intravenous chlorides which stabilized the blood chlorides and carbon dioxide, but did not control the toxæmia caused by the increased blood urea. (2) A fistula was made, but the major pancreatic and bile-ducts were transplanted into the jejunum, and hence the bile and pancreatic secretions were not lost through the fistula. The animals subjected to this operation lived and remained normal. (3) The pancreatic duct alone was transplanted. The fistula then discharged bile and duodenal secretions. These dogs also lived and remained normal. The conclusions of these experiments and observations are: "(1) Changes in the chemical reaction of the blood associated with acute duodenal fistula are chiefly the result of the loss from the body of the acid and chlorides of the gastric secretions through the fistula. (2) Even if the loss of the acids and chlorides in the gastric secretion from a duodenal fistula is prevented by gastro-jejunostomy, disturbance in motility in the upper intestinal tract causes an increase in the excretions of chlorides from the body through the intestinal and urinary tracts, with changes in the concentration of blood chlorides which are proportionately decreased. (3) Continuous loss of pancreatic secretion is fatal, whereas loss of bile and duodenal secretion is without lethal effect. (4) Disturbances of gastro-intestinal motility accompanying duodenal fistula apparently increase the excretion of chlorides from the body through the intestinal and urinary tracts."

One cannot be long in doubt about the development of a duodenal fistula. It may develop insidiously and show its presence by a slight bile-stained discharge. This, however, soon becomes more pronounced, as digestion of the sinus tract and excoriation of the skin rapidly follow.

A very efficient way of definitely proving the presence of duodenal fistula is by giving orally a capsule containing five grains of methylene blue. The dye will very soon appear in the discharge if a fistula has developed.

*Treatment.*—Treatment must be local and constitutional. Locally the wound must be treated by some one or combination of the recognized forms of treatment detailed below, and constitutionally, the chemical balance must be maintained.

By simple packing, the small fistula may heal readily. Usually, however, the fistula enlarges due to the digestion of the tract, and more efficient treatment must be instituted.

In cases where there is sudden increased intra-intestinal pressure which causes a large opening in the gut, there will be copious discharge at once, which comprises all liquids and food taken by mouth, as well as the secretions from stomach, liver and pancreas. This type is naturally a serious complication and calls for prompt, radical and courageous treatment.

If the discharge becomes profuse, the treatment given to Cases I and II, reported in this paper, should be used, that is, introducing a one-half-inch fenestrated rubber tube into the fistulous tract, the length of the tube depend-

ing on the depth of the fistula. This fenestrated tube acts as a reservoir and the discharge is removed from it by continuous suction. A water pump to furnish suction is the only practical apparatus, as all electric pumps become heated when in continuous use. It is very important to introduce the fenestrated tube, which is not directly connected with the vacuum bottle, as otherwise the tissue or large particles in the discharge will block the opening in the suction tip, and prevent the suction.

All food by mouth should be discontinued, moderate amounts of water may be allowed, as it does not stimulate the flow of digestive juices, and if the opening is not too large, a portion of the water will pass through and enter the gut below the opening. It also dilutes the discharge and keeps the suction working better.

Insulin has been mentioned by some of the foreign authors as being useful in reducing the amount of pancreatic secretion. They have not definitely proven this and we have had no opportunity to confirm or deny its beneficial effect. From a dietary standpoint, a low fat and low protein diet, theoretically, should reduce the activity of the pancreatic gland. In Fast's pancreatic fistula case, the secretion was measured and 120 cubic centimetres were discharged in twenty-four hours. The patient was then placed on high fat, antidiabetic diet, with no change in the amount of secretion. The diet was then changed to a high carbohydrate in the form of Karo syrup, given in two-ounce doses every four hours. This diet reduced the amount of the secretion to 60 cubic centimetres in twenty-four hours. There was no change, however, in the amount of excoriation of the skin.

Food may be introduced by nutrient enemata, glucose by vein or hypodermoclysis. If the patient does not become dehydrated, and remains in chemical balance, this treatment may be continued with expectancy of prompt healing. The excoriation of the skin rapidly disappears and the general condition of the patient improves.

In a recent article, "Experience with Venoclysis," Hendon<sup>3</sup> describes his technic and details the condition and treatment of a large number of cases suffering from various conditions requiring the introduction of food and fluid other than by oral administration. Briefly, his technic consists of inserting a permanent cannula into a vein, and introducing fluids and food continuously by slow infusion, giving 150 to 200 cubic centimetres per hour. We have had no experience with this method of treatment in cases of duodenal fistula, but have used it with gratifying results in other cases where food and fluids had to be introduced other than by the oral route, and we believe it would be an excellent way of treating a case of duodenal fistula, its chief points of advantage being, the length of time it may be continued, and the fact that at no time is there an excess of glucose or fluid in the circulation.

The treatment devised by Potter may also be used. We have not used this treatment, but have seen a patient so treated with satisfactory results. It is based on sound physiological principles, has been extensively used by

Potter and others in the treatment of duodenal fistula, and other high intestinal fistula with gratifying results. It can be used in conjunction with suction or any other form of treatment. Doctor Potter, in a personal communication, has kindly given us his present modified technic. Briefly it is as follows:

The easiest and best preparation of beef to use is one put out under the trade name of Bovinine, prepared by the Bovinine Company. It saves time and preparation, is packed in one-pound bottles, is sterile, thick and adheres well to skin and gauze. Soak the gauze in Bovinine until dripping and surround the fistula with it, but leave a crater in the centre similar to the hole of a doughnut. Fill the hole with about one to three drams of one-tenth normal hydrochloric acid solution, first introducing it with a dropper into the crater, as it is used up, surround the outside of the gauze with liquid adhesive or gutta-percha tissue made adherent to the skin through applications of chloroform. This keeps the beef-juice and acid confined to the area in which it is to be used and does not waste it. It is, however, an addition that may be omitted. The success depends upon keeping the skin surrounding the fistula from coming in contact with the pancreatic juice. Gauze carries the beef juice, the beef juice is digested by the pancreatic juice, the acid in the crater inactivates the pancreatic juice, but if there happens to be an excess it exhausts itself by digesting the beef juice rather than the protein of the skin.

Fast<sup>4</sup> reports a case of rupture of the pancreas, where the "pre-vertebral portion of the pancreas had been crushed against the anterior wall of the body of the vertebra, producing a V-shaped defect in the upper edge. Because of the extreme friability of the pancreatic tissue, suture was abandoned after one attempt." A drain was inserted with a subsequent pancreatic fistula which digested the tissue and excoriated the skin. This case was given Potter's treatment with complete healing of the pancreas and closing of the fistula fourteen days after this treatment was instituted, and the patient was discharged on the thirtieth post-operative day cured.

Another palliative treatment that may be used in conjunction with suction or with Potter's treatment is the passing of a duodenal tube through the mouth, stomach and well past the fistula. In this way the nutrition can be maintained by introducing food and fluid into the upper intestinal tube. Einhorn<sup>5</sup> reports two cases so treated. In Case VI, in this paper, an attempt was made to use a Reyfuss tube. The tube readily passed through the duodenum and passed the fistula, only to return through the gastroenterostomy into the stomach. Marogna<sup>6</sup> treated his case by visualizing the fistula at the ampulla of Vater, and passing a long rubber tube through the fistula down into the jejunum, using this channel for the introduction of liquid food.

The question naturally arises, why do these patients decline so rapidly? Colp<sup>7</sup> states: "The loss of fluids alone cannot account for the rapid emaciation and debilitation which occurs, for even though the body is supplied sufficiently with fluids, hypodermically, rectally or intravenously, and some

nourishment, admittedly small, is given by nutrient enemata, and the addition of glucose to the body fluids, deterioration occurs."

There is a loss of chemical balance due to the loss of the stomach, intestinal and pancreatic secretions, together with the formation and absorption of the toxins from the autodigestion. Case I illustrates this condition. Since a functioning gastro-jejunostomy was present, sufficient food and fluid could readily be given to furnish body requirements, yet the patient was critically ill during the few days of profuse duodenal discharge, which in this case consisted only of pancreatic and intestinal juice, with quantities of bile. The rapid pulse and anxious expression subsided synchronously with the subsidence of the discharge. No effort was made to reintroduce this lost secretion into the intestinal tube, as was done by Erdman,<sup>8</sup> where a jejunostomy had been done. In large fistulæ with copious discharge, we believe chemical balance will be restored more quickly if these secretions are reintroduced.

If the conservative treatment fails, and an operation is required, the following may be used: (1) Direct suture of the damaged area; (2) gastro-enterostomy with occlusion of the pylorus; (3) jejunostomy. All of these operations have been done by different authors who have reported cases with varying degrees of success. Let us briefly consider each procedure.

1. *Direct Suture*.—Due to the fact that we are dealing with a fixed portion of the gut, which is difficult to mobilize, and for this reason more difficult to properly close, direct suture is feasible in but few cases. When the defect is on the anterior surface, it is practically of no avail. The necrotic and digested gut does not heal and if one is lucky enough to make a closure, it invariably reopens, leaving the patient in a more deplorable condition.

In cases where the fistula follows a nephrectomy, or an injury, and the opening is on the posterior wall of the gut, the plan for direct suture suggested by Wm. J. Mayo<sup>9</sup> should be followed. Through an upper right rectus incision, the duodenum is exposed by retracting the liver upward and the transverse colon and hepatic flexure downward. An incision is then made through the peritoneum to the outer side of the duodenum and the bowel carefully separated from its posterior attachments. When the fistula opening is exposed, it can be easily and accurately sutured.

2. *Gastroenterostomy*.—This is an operation of considerable magnitude to be performed on as poor an operative risk as these patients of necessity are. It requires a general or spinal anæsthetic, and, to make it efficient, a pyloric occlusion must be done. There is also minimal danger of spreading infection. Giving of any quantity of food and fluid must be delayed for some hours. If, however, the operation is successfully performed, it meets the immediate indications and also offers an eventual cure, if the fistula is the result of an ulcer.

A simple and efficient way to occlude the pylorus is accomplished by placing a piece of fascia, either from *fascia lata* or from the rectus sheath, completely around the pylorus and tying it just as one would a silk ligature.

The efficiency of this form of occlusion has been demonstrated in doing gastroenterostomies with occlusion, for duodenal ulcer.

3. *Jejunostomy*.—The ease with which jejunostomy is done, the minimum of shock to the patient, the fact that it is usable at once to introduce fluid and food into the upper intestinal tract, the slight chance of infection in the wound, spontaneous closure when it is no longer useful, make this the operation of choice. McGuire,<sup>10</sup> Lewisohn,<sup>24</sup> Erdman,<sup>8</sup> Kelling,<sup>12</sup> and Pannet<sup>13</sup> have reported cases where it was used successfully.

COLP<sup>7</sup> abstracted and analyzed sixty-one cases of external duodenal fistula. He found "twenty-three to have followed operations on the gall-bladder, fourteen duodenal ulcer, ten nephrectomy, six resection of the stomach, six traumatic rupture of the duodenum, one carcinoma of the pancreas and one intestinal tuberculosis. In the entire group there was a mortality of 51 per cent. Thirty-six were treated conservatively with a mortality of 47 per cent. Twenty-five were treated by operative procedures with a mortality of 54 per cent. Fourteen cases of fistula which followed simple operations upon the gall-bladder had a general mortality of 15 per cent. Ten of these were treated conservatively with no mortality; four were operated upon, two successfully. In eleven cases in which the duodenum was opened, either at the time of operation, intentionally or accidentally, or found ruptured from external trauma, there was a mortality of 64 per cent. Eight were operated upon with a mortality of 85 per cent. and the three treated conservatively recovered."

"The fourteen cases which occurred after perforated duodenal ulcer, had a general mortality of 64 per cent. Of nine treated conservatively, seven died and of five treated by operation, two succumbed. Ten cases after right nephrectomy had a combined mortality of 50 per cent. Of six treated conservatively, three recovered and of the four treated by operation, one died."

#### CONCLUSIONS

In Cases I and II (treated by Bohrer) we believe the rubber dam was the real causative factor in the production of the fistula. The evidence is conclusive that a drain of any material inserted against a suture line in the duodenum is provocative of a fistula. (1) Acting as a foreign body, it has an erosive action. (2) Capillary drainage removes the lymph which biologically seals the suture line if not removed. (3) Prevention of adhesions to the suture line of the surrounding viscera, which if formed, would help seal it and increase its nutrition.

From the conclusions it follows, that if drainage is necessary, it should be so placed as not to come in contact with the suture line. In fact it should be placed and fixed as far as possible from the suture line.

#### SUMMARY

1. A drain down to the suture line of the stomach or duodenum should not be used. It is one of the causes of fistulæ.
2. The suction method is a simple and efficacious way to treat these fistulæ.
3. Chemical balance must be maintained.
4. Jejunostomy combined with suction is an operation of choice.
5. Gastroenterostomy with pyloric occlusion is a recognized procedure.



6. Potter's treatment is physiological and has been used successfully.
7. Insulin and proper diet theoretically should decrease the pancreatic secretions.
8. The best results have been obtained by conservative treatment in acute cases.
9. Operative treatment for chronic cases is imperative for cure.
10. Case XVII persisted for eleven years, and was cured by direct suture of the fistula.

## CLINICAL REPORTS

Seven cases of duodeno-cutaneous fistulæ are reported, also thirty-seven cases collected from the literature since 1923. A few cases were excluded due to insufficient data in case report to establish a diagnosis.

CASE I.—M. K., woman, fifty years of age, admitted to Bellevue Hospital September 25, 1924. Chief complaint that of pain in epigastrium, radiating to left and to back. Vomiting after every meal. She has lost thirty-four pounds in weight.

Abdominal section showed the stomach normal in size; on its posterior surface, near the greater curvature about 1 inch from the pylorus, there was a hard, indurated mass about 2 inches in diameter. It was not adherent to the posterior abdominal wall. There was considerable perigastric inflammation and adhesions, but no glands were palpable.

A pylorectomy with partial gastrectomy and posterior gastro-enterostomy was done. Due to a small amount of oozing a rubber dam drain was inserted, to remain for twenty-four hours. Patient returned to ward in good condition. Accidentally, the drain was not removed until the fifth day. The lower end was bile-stained. The following day there was definite bile drainage. This increased in amount and on the seventh post-operative day the abdominal skin was eroded from the irritating bile and intestinal secretion. The skin had been protected by vaseline gauze, and frequent dressings, but the area of erosion extended. The small sinus was then dilated and a one-half inch soft rubber fenestrated tube inserted, this acting as a reservoir. Into this large tube was placed a small rubber catheter attached to a vacuum bottle, the vacuum being maintained by a water pump, so that the discharge was removed as rapidly as formed and did not come into contact with the skin.

The eroded skin healed very quickly. The amount of discharge steadily decreased and the suction was discontinued on the tenth day. The sinus healed readily.

Since the patient had a gastro-enterostomy, the discharging sinus from the duodenum did not interfere with normal feeding and consequently she maintained her nutrition.

The patient was discharged from the hospital thirty days after operation. Had gained weight and had no stomach symptoms. She has been seen at three- to six-months intervals since that time, and has had no stomach disturbance except following marked indiscretion in her diet.

Following is an X-ray report of gastro-intestinal series made February 3, 1930, six years post-operatively. "The röntgenological examination of the gastro-intestinal tract made immediately, one, four, and six hours after the ingestion of a barium sulphate meal, shows the stomach to appear as a funnel. Hyper-peristalsis is present, the stomach being practically empty at the end of one hour, only a small amount of barium which has adhered to the sides of the walls is present. The head of the barium column at four hours appears to be in the splenic flexure, some barium still remaining in the small intestine. The six-hour examination shows the major portion of the meal in the cecum and ascending colon, some barium is seen in the transverse colon, the haustra of which is distorted, probably due to adhesions."

CASE II.—L. H., woman, age thirty, admitted to Knickerbocker Hospital, January 28, 1927. Chief complaint, pain in the epigastrium after eating. Symptoms of duodenal ulcer of four years' duration.

Abdominal section by Dr. Arthur Armstrong revealed the stomach normal in size and position; on the anterior surface of the duodenum just beyond the pylorus there was a small ulcer. The ulcer was excised and the gut repaired by the Horsley type of pyloroplasty. A rubber dam drain down to operative area. Convalescence was uneventful for first six days. Patient was allowed small amounts of fluid by mouth and received glucose solution by rectum. On sixth day wound was dressed and drain removed. Presently there was slight drainage of bile-stained fluid; the skin became excoriated. It was evident that a duodenal fistula had developed. It was treated for the first two days by protecting the skin with paste. This did not prevent skin excoriation. Although there was considerable drainage, all of the stomach and duodenal contents could not have been discharged through the fistula, as the patient did not become dehydrated and she maintained her nutrition very well. On the ninth post-operative day, the sinus was enlarged sufficiently to permit the introduction of a one-half inch fenestrated tube. This acted as a reservoir and a small catheter was put inside this tube and attached to a vacuum bottle. The discharge decreased rapidly. All food was discontinued by mouth, although the patient continued to take enough water to control her thirst. She received glucose solution by rectum. The suction was discontinued on the fourteenth post-operative day. The sinus healed kindly.

CASE III.—T. S., male, age sixty-one, admitted to Bellevue Hospital, October 24, 1925, for treatment of pyloric obstruction.

At abdominal section done November 6, 1925, the stomach was found normal. Pylorus, duodenum and great omentum were adherent to anterior margin of the right lobe of the liver, and the round ligament. Walled in by these adhesions there was an abscess cavity containing about 16 ounces of thick yellow pus, and some small calculi. A portion of the gall-bladder had sloughed away and the remainder of it was adherent to the duodenum. Cystic duct, foramen of Winslow and hepatic vessels could not be identified. Under local anæsthesia, an upper right rectus incision was made. The abscess cavity was opened by freeing omentum from edge of liver and fluid removed by suction. Considerable hæmorrhage was encountered and controlled by gauze pack. Rubber dam drain to bottom of the abscess cavity.

November 7.—Sero-sanguinous discharge with some bile. November 9.—Very little post-operative reaction. Profuse sero-sanguinous discharge stained with bile. Most of gauze pack removed. Culture taken at operation shows staphylococcus aureus. November 10.—Has foul smelling discharge. Patient has developed a duodenal fistula. November 11.—Transfusion of 500 cubic centimetres of blood. November 13.—Jejunostomy was done on account of profuse discharge and dehydration. Suction to remove discharge from fistula. November 16.—Suction working well. Jejunostomy satisfactory, but patient very weak. November 20.—Patient died.

CASE IV.—W. H., male, age fifty-three, admitted to Bellevue October 20, 1922. For past eight weeks has had pain in upper abdomen with nausea and vomiting and belching of gas. Pain lasts two to three hours and does not radiate. An indefinite mass is palpable in the right upper quadrant. At operation October 23, 1922, in the right upper quadrant was found a collection of greenish fluid, 1½ quarts, having odor of gastric content. It was well encapsulated by surrounding viscera and omentum. One inch from pylorus there was a perforated duodenal ulcer, 1 centimetre in diameter, from which stomach contents exuded. Stomach and gall-bladder normal. The opening into the duodenum was closed with five interrupted chromic sutures. A portion of adjacent peritoneum was then used to cover the suture line. Posterior gastro-enterostomy was then done. Cigarette drain down to site of perforation.

October 24.—There is a greenish discharge from wound. October 25.—Profuse bile-stained fluid. Drain loosened and large catheter inserted to bottom of wound for

water suction. Discharge too thick to be removed by suction. October 26.—Discharge bile-stained and profuse. Skin becoming excoriated. October 29.—Drainage almost pure bile. Digestion of tissue very marked. October 31.—Profuse discharge of bile. November 2.—Patient died.

CASE V.—P. H., male, age forty-one, admitted to Bellevue Hospital, November 9, 1925, for treatment of duodenal ulcer as shown by continuous pain in right upper quadrant for past two weeks, and frequent vomiting and loss of weight, with tarry stools, distention and tenderness in epigastrium. Mass felt on deep palpation of epigastrium. Transfusion November 23.

Abdominal section November 25 revealed an ulcer on the posterior surface of the lesser curvature three inches above the pylorus. There was also an ulcer on the anterior surface of the first portion of the duodenum, which was the source of hæmorrhage. There was also a second healed duodenal ulcer three-quarters of an inch distal to the bleeding ulcer.

The bleeding duodenal ulcer was incised with a cautery, and the duodenum opened inward to explore the other ulcers. The duodenum was then closed with a lockstitch, and posterior gastro-enterostomy was done.

December 1.—Discharged large amount of gastric contents through wound. December 2.—Thin profuse discharge through small sinus in upper angle of wound. December 3.—Transfused 500 cubic centimetres. December 4.—Profuse duodenal discharge. Jejunostomy under local anæsthesia. December 5.—Jejunostomy tube in place. Condition very poor. Profuse discharge. Dehydrated. December 7.—Has improved. Suction working well. Fed through jejunostomy. December 11.—Patient continues weak. Clysis of 1000 cubic centimetres of saline. December 18.—Patient became weaker and died.

CASES III, IV, and V were treated in the First Surgical Division, of Bellevue Hospital, service of Dr. John Alexander McCreery, through whose courtesy these cases are reported.

CASE VI.—M. S., female, admitted to Bellevue Hospital in the service of Dr. Carl Goodwin Burdick, February 14, 1930. Chief complaint: pain in right upper quadrant for past three weeks. Surgical history: in 1922 had a pelvic operation; 1925, cholecystectomy and adhesions. Present illness: About one and a half years after cholecystectomy, the woman again began to have gastric disturbance with pain in right upper quadrant. This pain radiated to right breast and right shoulder. Occurred a half to one hour after meals and occasionally at night. Has been nauseated but rarely vomited until the past three weeks. For past three weeks pain has been more severe and continuous. For past week patient has vomited two to three times per day, unable to retain food or water. Slight streak of blood at times. No tarry stools.

Abdominal section was performed February 28. In the second portion of the duodenum was an area of induration located on posterior surface, densely adherent to pancreas and believed to be an ulcer perforated into pancreas. Posterior no-loop gastroenterostomy was done. No drains. Aftercourse of convalescence attended with broncho-pneumonic symptoms involving bases of both lungs.

March 17.—Area of redness and tension has developed at the lower angle of wound. Upon incision expelled gas and intestinal contents. A duodenal fistula has apparently formed. Drainage instituted. March 18.—Reyffuss tube in stomach. Water suction for wound. Skin excoriated. March 25.—X-ray to locate position of Reyffuss tube shows it to pass through duodenum, back through gastroenterostomy and into stomach. Suction working excellently. March 30.—Greatly improved. Less drainage, but there is swelling and tenderness in right lower quadrant. Temperature elevated. April 1.—Incision under local anæsthetic of swelling in right lower quadrant; pus and gas evacuated. Abscess well walled off. April 3.—Temperature down. Very little drainage from fistula. April 12.—General condition good. Duodenal fistula completely closed.

CASE VII.—V. F., male, aged forty-two, admitted to Bellevue Hospital March 8, 1928, to service of Dr. George David Stewart, on account of an abdominal fistula. His past history was of a gall-bladder operation February, 1927. He was told that he had an echinococcus cyst. July, 1927, he became jaundiced, had biliary colic, was operated on and gall-bladder removed with one large stone in cystic duct. Following this there was a yellow, purulent discharge. Five weeks prior to present admission to hospital, he noticed particles of food in the discharge that came from his sinus. The man was emaciated and looked chronically ill, otherwise physical examination was negative except for local condition. There was the cicatrix of an upper right rectus incision, in the middle of which there was a fistula, the discharge from which was brownish in color and contained particles of food.

March 18.—Methylene blue was given by mouth and this promptly appeared through the fistula and stained the dressing. March 20.—Radiographic examination revealed a duodenal cutaneous fistula which communicated with the second portion of the duodenum.

At operation, March 30, there was a mass of adhesions about the gall-bladder region, consisting of great omentum, liver, duodenum and stomach. The duodenum could not be isolated due to this dense adhesive mass. There were no palpable masses in the liver. A gastroenterostomy with pyloric occlusion could not be done on account of the above-described adhesions. A jejunostomy was then done, inserting a catheter into the gut.

April 6.—Still slight discharge from the duodenal fistula, the jejunostomy working well. Patient being fed entirely through this tube. This treatment was continued until April 28, when the jejunostomy tube was removed, the duodenal fistula closed, patient allowed to take food by mouth. He was discharged May 19, 1928, entirely well with the fistula healed.

#### ABSTRACT OF CASES OF DUODENO-CUTANEOUS FISTULÆ REPORTED IN LITERATURE SINCE 1923

WEBB.<sup>14</sup>—Man, aged sixty-two. X-ray showed almost complete obstruction at pylorus. Operation revealed tumor about 3 centimetres in diameter at pylorus. Lower third of stomach and about 2 inches of duodenum resected. Posterior gastroenterostomy done. Drain inserted into the lesser peritoneal cavity. *Post-operative diagnosis.*—Peptic ulcer at gastro-duodenal junction. Drain removed third day; in ten days, stitches removed, wound entirely healed. Eighteen days after operation patient vomited small amount of fluid containing bile. Upper part of incision opened and discharged enormous quantities of yellowish fluid. Everything by mouth discontinued. Patient given glucose and soda solution continuously by rectum. Skin smeared with thick ointment containing camphor phenol. Dressings changed as fast as they became moistened by drainage. Sixteen days later fistula was entirely closed.

GARDNER.<sup>15</sup>—Woman, aged sixty, who had repeated attacks of knife-like pains referred to right shoulder. Operation disclosed mass of adhesions tying up gall-bladder, stomach, duodenum and omentum. Running from fundus of gall-bladder to duodenum was a fistula about the size of a lead pencil, and imbedded in the fistula about one-half inch from gall-bladder was a stone about the size of a large pea. This was milked into the gall-bladder. Dense adhesions obscured common duct which was evidently obliterated. Removed two stones and as gall-bladder was not acutely inflamed, sutured it up tight, closed with great care. By fifth post-operative day lobar pneumonia had developed. For nine days the wound discharged profuse thick, foul pus, which later became thin and excoriated skin. This discharge persisted for a month when the patient finally convalesced and went home. At end of a year post-operatively she

reports two or three attacks of pain in the epigastrium going through back, also gall-bladder region. Lasts twenty-four hours. Feels perfectly well between attacks.

LAHEY<sup>16</sup> reports two cases of duodenal fistula successfully treated by suction. One patient gave history of pain in right upper quadrant, rapid onset followed by quite acute tenderness in the right hypochondrium. He was operated upon and found to have duodenal ulcer, around which walling off had taken place with production of small subhepatic abscess. As a result of drainage of abscess a duodenal fistula developed.

In the second case a calloused pyloric ulcer was removed by pylorotomy, anticolic anastomosis by the Polya method. Three months later, patient developed a tender spot in his wound, which, when opened, discharged a thin, watery material that soon digested the surrounding skin and converted the sinus into one which was rapidly and progressively enlarging. After twenty-one days of suction the sinus was closed.

PARSONS<sup>17</sup> reports case of male, aged forty, who in August, 1927, had profuse hæmorrhage from stomach. Operation done October, 1927, under local anæsthesia, revealed a large, penetrating ulcer of the anterior wall of the stomach firmly attached to the abdominal wall, difficult of mobilization. Subtotal gastrectomy was performed, supplemented by posterior gastro-enterostomy. For seven days post-operative drainage from wound. Aspirated. Eighth day, Potter treatment instituted, substituting dilute acetic acid for hydrochloric. Wound dressed at intervals of two hours. Twenty-three days post-operative a small fistula, of the part of the stomach that remained, developed and this was closed by means of a pursestring suture, plus an interrupted row of Lembert. Discharged from hospital on thirty-sixth day post-operative.

POTTER<sup>18</sup> reports three cases. First, male aged forty-five. Operation revealed a large callous duodenal ulcer about 3 centimetres in diameter on the anterior wall of the duodenum, adherent to the lower surface of the liver. Ulcer was closed by purse-string and No. 1 chromic gut. Abdomen closed in layers with two small drains in abdominal incision, one extending down to site of ulcer. Drain removed on seventh day and on ninth day after operation it was noticed abdominal wall was breaking down. A duodenal fistula developed which discharged pancreatic juice and bile. Secondary suture was done, but on seventh day after closing duodenal fistula, the wound again showed evidence of digestion. Continuous suction was attempted but did not check destruction. Beef-broth-olive-oil and one-tenth hydrochloric acid solution then used with complete cure.

Second, a case operated on for supposed acute, perforated appendicitis. At operation the appendix was found to be slightly congested, and the right lumbar gutter and pelvis were filled with chylous fluid. Two large drains were inserted, and the abdomen closed. During the next twenty-four hours, the dressings had been saturated very often, and at the end of that time the abdominal wall showed the usual digestion from pancreatic juice. The condition was a perforated duodenal ulcer. Hypodermoclyses of salt solution and dextrose were given twice daily, and the wound was surrounded in its entire length with gauze soaked in beef juice. A trough was left in the centre, and long strips of gauze, dripping in tenth-normal hydrochloric acid, were laid directly over the entire length of the wound and changed every hour. The wound had practically healed in twenty-six days. There had been no attempt to close the duodenal ulcer. Without a suture whatsoever to close the perforation, the fistula healed with the treatment described.

Third.—Man, aged twenty-nine, had a perforated duodenal ulcer and evidence of a spreading peritonitis that made it necessary to invert the ulcer and stitch a piece of omentum to the suture line. The perforation was the size of a pea. There had been considerable spill. About the eighth day after the first operation the abdominal wall appeared irritated and the dressings were saturated with pancreatic juice. Beef-juice and acid treatment was instituted, and the fistula healed in eleven days. Four weeks after the first operation the abdomen was again opened. The site of the old perforated duodenal ulcer, with its healed duodenal fistula suture line, had plastered itself to the

abdominal wall at the site of the primary right rectus incision and had healed in that location. At the second procedure a posterior, no-loop gastroenterostomy was done, without disturbing the site of the previous operation. The wound was closed without drainage, and the patient made an uneventful recovery and has remained well ever since.

WARSHAW.<sup>10</sup>—A woman, aged fifty-five. At operation a small, partially gangrenous, suppurating gall-bladder was found, wrapped almost completely with suppurating omentum. On attempting to dissect the omentum away, the operator opened into an abscess cavity leading down to the dome of the gall-bladder which was almost completely destroyed. An ounce of thick, green pus and about a hundred white stones of various sizes were evacuated. After removal of the pus and stones, a rubber tube drain was sewed into the gall-bladder with a pursestring suture. Two cigarette drains, one to the foramen of Winslow and one to the right lumbar gutter, were also inserted. After four weeks of moderate temperatures and progressive wound-healing, symptoms of intra-abdominal infection began to develop. Exploration opened into a cavity just posterior to the anterior abdominal wall which contained a large amount of foul pus and necrotic material resembling omentum, together with particles of food such as peas, spinach and milk curds, all stained with golden-yellow bile. A fistula admitting a finger was discovered leading into the jejunum apparently close to the duodenum. A profuse flow of alkaline, semi-fluid intestinal contents mixed with pus rapidly attacked the enlarged wound and surrounding skin. In twenty-four hours so much digestion of abdominal wall had occurred that the crater was double its former size and the fistulous opening into the jejunum at the bottom of the crater had increased proportionately. The patient began to look haggard; she was failing alarmingly. Potter's treatment was used and the patient recovered.

RAZZABONI<sup>1</sup> reports case of a woman, aged forty-nine, who had been suffering for months from some form of infective biliary calculus which caused a permanent icterus which was more accentuated after attacks of colic from which she suffered frequently. June 20, 1926, a right para-rectal laparotomy was performed. This revealed a compact mass of hepato-entero-epiploic adhesions in the region of the gall-bladder. The gall-bladder was reduced to a minimum size; a large calculus was detected beneath it. This was located probably in the common bile-duct. While these adhesions were being separated a vessel of the duodenal wall was injured which was immediately ligated. After the extraction of the calculus the operation was completed with drainage for which purpose a large Kehr tube was used. The post-operative course was regular in the beginning and no disturbance seemed to follow the removal of the drainage tube on the tenth day. On the fourteenth day from the date of operation there occurred an abundant discharge from the operative wound; the bile discharge was as usual but there was a discharge of grayish liquid mixed with alimentary contents which was very abundant. The discharge of this liquid became more abundant on the following days and was uninterrupted and caused loss of strength and weight. This course finally took a fatal turn and death of the patient followed in a condition of pronounced marasmus, six days after the first abundant discharge.

PATEL and CARCASSONE<sup>20</sup> report case of R. M., twenty-nine. Operation for duodenal ulcer; posterior gastroenterostomy. Excision of ulcer. Eleven days after operation a suppurating mass was noticed under the incision. On opening the mass, a large amount of duodenal liquid was found; exploration revealed a small duodenal fistula, the opening of which could be visualized. Rapid emaciation of patient with marked digestive action of liquid on skin; patient vomited incessantly. Twelve grams calcium chloride given; nothing by mouth, glucose intravenously, nutritive enemas, Murphy drip. Skin protected with double layer of zinc oxide applied every hour. Fluids allowed at end of forty-eight hours, fractionally and repeatedly; also daily injections of 15 units of insulin. (It renders discharge less toxic.) Patient's general condition improved steadily; discharge ceased in ten days and in fifteen days patient went home cured.

MAROGNA<sup>6</sup> reports case of man, aged forty-five, who had a nephrectomy for nephrolithiasis and kidney abscess. Gauze drain removed on fourth day was found stained with bile and covered with curdles of milk injected the day before. Methylene blue given by mouth appeared in wound within a few minutes. Exploration showed a duodenal fistula easily visualized and about the size of a dime; it was a few centimetres below the ampulla of Vater. Rapid emaciation of patient with marked digestive action of skin about wound. Long rubber tube pushed down into jejunum through fistula, and glucose solution and milk with yolk of egg nutrient enemas, Murphy drip and glucose intravenously. Marked improvement in patient's general condition. On the eighteenth day of this treatment, secretion stopped almost completely. Simple extra-peritoneal suture of fistula was tried as the simplest method. Nothing by mouth for two days, hypodermoclysis, nutrient enemas for three days; no leakage. On eleventh day after operation patient was discharged cured.

RIGBY<sup>22</sup> reports seven cases. No. 1, hurt by a fall while playing football. Exploration revealed traumatic perforation of second portion of duodenum. Perforation sutured and peritoneum and omentum were sutured over it. Drain tube passed through a stab wound in right lumbar region, down to renal pouch. Fourth day post-operative definite duodenal fistula. Skin became excoriated. On eighth post-operative day was reopened. Posterior no-loop gastro-jejunostomy was done. Pylorus occluded by a pursestring suture of silk. Recovery.

No. 2.—Nephrectomy for right pyonephrosis. Wound was drained. Wound healed and patient discharged. Wound was opened two months later on account of pain and copious discharge of thick, yellow fluid. Skin excoriated and painful. This discharge continued for two months. Treatment frequent dressings and emollient to protect skin. Recovery.

No. 3.—Appendiceal abscess of ten days' standing. Operated and drained with two tubes and gauze. Appendix not removed. When tubes and gauze were removed three days post-operatively, a large amount of thin, sour fluid containing bile was discharged. Treated with operation. Recovery.

No. 4.—Acute diverticulitis of duodenum. Reported in *Lancet*, 1923. An inflamed and partly gangrenous diverticulum was found in the mid-portion of the duodenum and was excised. Third day post-operative wound discharged brownish watery fluid. This was never profuse. Recovery.

No. 5.—Operated for subhepatic abscess. Duodenal fistula developed and continued for eleven years. General health was never much impaired, but skin was always somewhat inflamed and at times discharge was copious. Operated by closing fistula in first part of duodenum. No further leakage.

No. 6.—Partial gastrectomy for carcinoma of stomach. Patient made good recovery. After discharge from hospital, wound discharged alkaline, bile-stained fluid. Local treatment resulted in cure.

No. 7.—Operated for carcinoma of lesser curvature of stomach. Partial gastrectomy was performed. Twenty-three days post-operative wound discharged bile-stained fluid. Treated conservatively with closure of fistula.

SALMON and GAMBILL<sup>23</sup> report case of male aged fifty-six, operated for perforated duodenal ulcer. Soft tube drain. Seventh day post-operative had a discharge. Nutrient enemata. Skin treated with zinc ointment and zinc stearate powder. Water suction. Treatment discontinued on the seventh day. Recovery uneventful.

WORTHEN<sup>24</sup> reports case of male, aged thirty-eight, operated for perforated duodenal ulcer. Developed empyema right side. Rib resection. Operation for rib resection established through and through drainage from chest to abdomen for a subphrenic abscess and the empyema, one operation followed by pneumonia. Case later complicated by lung abscess, a bronchial fistula and various transfusions. One year later taken to hospital, sinus still draining. With lipiodol X-ray revealed duodenal fistula. Laparotomy was performed avoiding abdominal sinus opening. Stump of this

fistula was inverted with a pursestring. In three months drainage diminished and ceased. At present time in robust health.

LEWISOHN.<sup>24</sup>—Woman, aged fifty years; cholecystectomy three years previous; February 22, 1930, laparotomy under spinal anæsthesia; extensive adhesions; accidental opening into the duodenum, sutured. Common duct found compressed by mass at porta hepatis; drainage tube from common duct to external surface which drained well; two days later duodenal contents appeared in the discharges; jejunostomy; suction apparatus in previous operative field with protection of skin by zinc oxide and talcum powder; profuse drainage through suction apparatus which stopped after two weeks. The drain fluids were reintroduced through the jejunostomy tube; subsequent course stormy; improvement after citrate transfusion. At end of three weeks jejunostomy tube removed; immediate spontaneous closure in opening of jejunum; rapid general improvement; discharged April 10, 1930. Death six months later, exact cause unknown.

LAFOURCADE.<sup>52</sup>—M. H., forty-three, perforated duodenal ulcer. Operated upon May 6, 1927. Large ulcer mesial side of second portion of the duodenum, surrounded by a callous border. Pylorectomy, subhepatic drain. Dressings stained with bile on sixth day and within twenty-four hours there were marked digestive signs of skin about wound. Supportive and protective treatment for twenty days. Discharge till now contained gastric and pancreatic juice; suddenly patient grew worse; became markedly dehydrated, very emaciated and semi-comatose within three days. These symptoms were synchronous with a stoppage of pancreatic contents in the discharge as shown by the color of the discharge and a change from alkaline to acid reaction. Injections of one ampule of insulin on May 31, repeated at night, were followed by marked improvement in subjective symptoms. Two injections each following day. Remarkable general and local improvement and on twelfth day only a small fistula remained discharging only slightly at intervals. June 10, gastroenterostomy with occlusion of pylorus. Complete cure in two weeks.

MOULONGUET<sup>26</sup> reports a case in which there was an operation for perforated duodenal ulcer. Suture of perforation; gastroenterostomy. Drainage. Small fistula occurred after discharge of patient from hospital, and persisted for seven months. Operation revealed an extensive induration at the site of the fistula and a marked stenosis of the duodenum. Removal of entire anterior portion of first part of duodenum. Complete cure. Patient discharged in fifteen days.

GAMINARA.<sup>27</sup>—Patient, seventy-five years old. Subtotal gastrectomy for cancer of pylorus; on the ninth day when the stitches were removed a slight inflammation of the skin was noticed and the next day a clear alkaline fluid appeared on the dressings having marked digestive action on the skin; during the next two days the opening in the skin became larger and about 150 cubic centimetres of this fluid was obtained in the twenty-four hours. A siphon was applied four days after its appearance and was left in place for twelve days; fistula healed in nineteen days.

JOHNSON.<sup>28</sup>—Two cases: First case.—Choledochoduodenostomy. Developed a large duodenal fistula with rapid emaciation and decline. Abdominal skin became excoriated. Treated by injecting into the fistula a 1 per cent. solution of citric acid, two to three ounces, three to four times per day. Complete healing in ten days. Recovery.

Second case.—Cholecystectomy. There were two stones in the gall-bladder and one in cystic duct. Due to an anomaly of the cystic duct, the common duct was apparently divided. Later operation performed for choledochoduodenostomy (Mayo) around a six-inch length catheter. Wound drained. Four days later developed a duodenal fistula. Treated with citric acid same as Case I. Fistula healed in eighteen days. Recovery.

GILBRIDE.<sup>29</sup>—Operation for duodenal ulcer. Ulcer excised with cautery and posterior gastroenterostomy. Abdominal wound apparently healed *per primam*. On tenth day when sutures were removed about 200 cubic centimetres clear fluid evacuated. Methylene blue given by mouth appeared on the dressing in three-quarters of an hour.



Author states there was a crater-like opening in the duodenum, twenty-five days post-operative. We assume that the case terminated fatally; author does not state.

GIBBY.<sup>30</sup>—Cholecystectomy; four days post-operative duodenal fistula developed. Continuous discharge with marked irritation of the skin. Wound reopened and injury repaired with linen sutures. Improved for a few days then fistula reopened. In two days patient's condition seemed desperate. Abdomen opened for the third time. Closure was impossible so omentum was drawn up and sutured into the fistulous opening. Result was slight duodenal discharge persisting for several days which gradually stopped and patient made good recovery.

WALTMAN.<sup>31</sup>—Choledochoduodenostomy. Duodenal fistula developed on seventh post-operative day. Blood changes consisted of decrease in chlorides and increase in urea. Toxæmia was treated by intravenous solution of sodium chloride. This case had an acidosis due to disturbed liver function from the obstruction. This was shown by low carbon dioxide combining power of blood. Glucose added to infusion was given for this condition. Wound treated by suction and fistula closed on seventh day after appearance of fistula. Patient discharged cured.

WALTERS and BALLMAN<sup>2</sup> quote a case treated by Judd<sup>11</sup> of duodenal fistula following resection of stomach with Balfour-Polya anastomosis for carcinoma of stomach. Suction was used to keep the fistula dry. Blood chemistry before operation was, chlorides milligrams 522 and urea milligrams 21. Subsequent to development of fistula chlorides dropped to 327 milligrams and urea rose to 84 milligrams. This case was not given intravenous sodium chloride. Resulted fatally.

ALEXANDER.<sup>32</sup>—Perforation of first portion of duodenum through an old callous ulcer. Perforation closed and gastro-hepatic omentum sutured over it. A tube was inserted both in Morrison's pouch through a right stab incision, and in the pelvis. Tubes removed on sixth day. Nine days post-operative frank duodenal fistula draining through stab wound in flank. Skin became excoriated in next twenty-four hours. Eleven days post-operative a duodenal tube passed by mouth and feeding started. Thick pads of gauze were strapped tightly over the opening of fistula. This reduced the discharge. Thirteen days post-operative X-ray showed duodenal tube curled up in stomach. It was removed. Treatment continued. Twenty days post-operative gradual decrease in discharge. Twenty-five days post-operative fistula closed.

LICK.<sup>33</sup>—Perforated duodenal ulcer with adhesions between gall-bladder and liver, near the terminal portion of the second part of the duodenum. Perforation approximately opposite the opening of common duct. Due to immobility and inaccessibility closing was very difficult. Posterior gastroenterostomy. Cigarette drain with only rubber at lower end placed down to perforation. Duodenal fistula developed on fourth day, discharge was copious and foul smelling. Fifth post-operative day entire wound open, drainage profuse. Aspirations of wound by suction through catheter. Death from inanition and exhaustion on the ninth post-operative day.

CASE.<sup>34</sup>—Tuberculosis of gall-bladder with dense adhesions about the gall-bladder which contained a large stone. Cholecystectomy with drain to cystic duct. Stomach and duodenum normal except for adhesions. On sixth post-operative day duodenal contents were found in drainage. Carmine given by mouth appeared in the discharge from fistula. Skin was protected with charcoal. Intravenous injections of glucose and Ringer's solution were repeatedly given. Suction was used but to no avail. On twenty-first post-operative day a duodenal tube was introduced well into the upper jejunum. The drainage diminished at once. On the thirtieth post-operative day and nine days after introduction of tube, it was removed. Patient recovered.

ROTH.<sup>35</sup>—A man, forty-four years, into whose epigastrium, a little to the right of the mid-line, a splinter of wood had been forced. The splinter had been removed by a comrade. Abdomen rigid and liver area very painful. Laparotomy disclosed bloody fluid in peritoneal cavity; a tear in the liver; a tear in the second portion of the duodenum 2 centimetres long from which exuded bile-stained fluid. There was a second

## DUODENO-CUTANEOUS FISTULÆ

tear lower and more lateral. Both wounds were sutured and the area drained. Fifth post-operative day there was a discharge of bile and duodenal contents, which excoriated the skin. Protective dressing. On twenty-first post-operative day fistula was healed.

GRUENFELD and SEGOLOFF.<sup>36</sup>—In 1922 cholecystectomy with transperitoneal exploration of right kidney. Immediate post-operative course uneventful. Two weeks after discharge from hospital, developed abscess in right lumbar region which after incision and drainage, healed in ten weeks. A second abscess at end of one and a half years, which was incised and drained; this incision did not completely heal. At end of three years there was still a very slight discharge from the sinus. Methylene blue was injected into sinus and the dye was found in the vomitus. By X-ray and injection of dye and iodized oil, a definite diagnosis of duodenal fistula was established. The pathology of its development could not, however, be determined. Due to the slight inconvenience of the fistula no curative treatment was instituted.

WINKELBAUER.<sup>37</sup>—Man, fifty-one years, partial cholecystectomy for gangrenous fundus of gall-bladder. Due to the poor condition of patient, the gangrenous portion of the gall-bladder was cut away, three stones removed and drain down to base of gall-bladder. Developed fistula which was still active when patient was discharged from hospital one and a half months later. Readmitted to medical clinic with cardiac asthma, where patient died. Post-mortem showed coronary sclerosis and myocardial changes. There was a "Y"-shaped fistula, one arm of which communicated with the shrunken gall-bladder which contained one stone and the other arm entered the duodenum three centimetres from the pylorus. There had, however, been no discharge of duodenal contents.

Of the forty-four collected cases in this paper, the total mortality is 18 per cent. Twenty-one cases were operated upon for gastric or duodenal ulcer. Of these, four died. Of four operated upon for gastric carcinoma, three recovered from the fistula. Thirteen cases were operated upon for disease of the biliary tract (one of this number having tuberculosis of the gall-bladder), ten recovered and three died. Two cases had nephrectomies; both were treated conservatively with recovery. One case of acute diverticulitis of the duodenum, one case of subhepatic abscess, and two cases of rupture of the duodenum. All recovered.

If we add the sixty-one cases collected by Colp up to 1923, we have 105 cases in all, with a combined mortality of 37 per cent. Forty-six cases were operated upon for disease of the stomach or duodenum. Thirty-five were operated upon for disease of the biliary tract. Twelve nephrectomies; eight traumatic ruptures of the duodenum; one carcinoma of pancreas; one intestinal tuberculosis; one diverticulitis of duodenum; one subhepatic abscess.

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# INTUSSUSCEPTION IN AN ADULT

ASSOCIATED WITH ADENOMA OF ILEUM

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THE occurrence of intussusception in adults is relatively rare as compared with the incidence of the same condition in early life. In consequence the diagnosis is difficult and the condition is not easily differentiated from other forms of intestinal obstruction.

Whereas absence of discernible etiological factors is the rule in intestinal intussusception in children, the reverse is more generally the rule in later life. Perhaps the relative frequency of its incidence during the first year is due to the disproportion in calibre between the large and small bowel at the ileocæcal region, which is greatest at this time of life. It is believed by some that when the ileum joins the colon at an angle of greater than  $90^\circ$ , intussusception is more likely to occur. Furthermore, when the ascending colon has a mesentery, the intussusception may ascend high up; and, when there is no mesentery the process usually stops at the ileocæcal valve. The mobility, capacity and flaccidity of the cæcum, and the undue length of the meso-colon in these cases afford favorable conditions for the invagination to occur. Thus, in an extensive and intensive analysis of this disease undertaken by Elliot and Corscaden in 1911, the following classification of etiological factors in 300 cases was noted:

1. Those cases associated with benign tumors.
2. Those cases associated with malignant tumors.
3. Acute cases without demonstrable cause.
4. Those cases associated with ulcers of typhoid, dysentery, tuberculous and other origins.
5. Subacute and chronic cases without demonstrable cause.
6. Subacute and chronic cases with intrinsic pathology of the intestine such as tuberculous infiltration.
7. All cases associated with Meckel's diverticulum.

Of the cases with coincident pathology of the intestine definitely evident, those placed in the category of cases associated with benign tumors of the intestine formed by far the predominant number. Sixty or one-fifth of the total number analyzed were thus classified. Of this number, the greater part were found in the small bowel with the ileum the site of predilection.

While benign tumors of the small intestine are being reported with increasing frequency, their occurrence is yet sufficiently rare to warrant note

being made of individual cases. Thus King states that only eight cases of true solitary tumor of the small bowel were found in 44,654 laparotomies at The Mayo Clinic. Ferguson found eight benign tumors of the small bowel in 3,327 autopsies at the Massachusetts General Hospital. Mallory reported eleven such tumors in 4,165 autopsies at the Boston City Hospital. King notes the order of frequency of the types of tumor found as myomata, lipomata, adenomata, fibromata, angiomata, fibromyomata, neurofibromata and cysts.

Intestinal benign neoplasms may be present without causing symptoms of any kind. This is especially true if the tumor is small. In the latter case it may be an incidental and accidental finding in a laparotomy undertaken for another condition, or may be found at autopsy in case of death from other cause. Even somewhat larger tumors may be unproductive of symptoms if growth takes place toward the serosal surface, provided no pressure phenomena are exhibited. However, when growth takes place toward the lumen of the gut, symptoms of obstruction, hæmorrhage, or, more frequently, intussusception may occur. Thus in a series of forty-five cases of fibromata of the intestine reported by Clifton and Landry, thirty-three were associated with intussusception, of which number twenty-two were in the small intestine.

The relationship between tumors of the small intestine and the occurrence of intussusception has been productive of much speculation. Various explanations have been advanced to explain the causal relation of the one to the other. Of these the greatest agreement appears to centre about the following:

1. Mere weight and pull of the tumor by means of which that portion of the intestine attached to the tumor is dragged into the succeeding section of gut.

2. Violent peristalsis due to foreign body reaction. This explanation differs from the preceding in that the process is regarded not as a passive one, but as an active one. The tumor is regarded as being dragged along by the hyperactive peristalsis of the intestine initiated by the presence of the tumor itself. The attached intestine being pulled along with the tumor, intussusception occurs.

3. In opposition to the above theory, Wardell has pointed out that the tumor is often at some distance from the apex of the intussusceptum. In explanation of this, he modifies the previous account of the course of events. He regards the origin in these cases as resulting from spasm of the gut around the site of the tumor, with relaxation distal to it. Thus "conditions are favorable for the final act of peristaltic gymnastics whereby the constricted part is induced to slip into the dilated portion" of intestine. In this connection, it is interesting to note, Lindsey and Perrin, quoted by Wardell, attempt to adduce the same explanation to account for the mechanism of intussusception in children. According to these authors, inflamed lymphoid tissue of the intestine is productive of an intestinal

reaction similar to that described above, the place of the foreign body in this case being taken by the inflamed tissue. Wardell warns of the danger of overlooking an intestinal tumor at operation due to its distance from the apex of the intussusceptum. He advises careful palpation of the proximal healthy gut in all cases of intussusception over the age of two.

4. Perverted muscle action due to the presence of the tumor has been advanced as a cause of the origin of this condition.

5. Paralysis of the bowel is yet another theory adduced in explanation of intussusception in these cases.

The occurrence of intussusception in adults may be associated with acute or chronic symptoms. Acute symptoms are those of acute intestinal obstruction, usually, although not always, associated with a palpable mass. The presence of blood in the stools and a palpable mass by rectum are not constant. The occurrence of a bloody stool is far less frequent in adults than in children. When present it is usually due to torsion or ulceration of the tumor. One would, however, expect with twisting of the mesentery, symptoms of acute strangulation to rapidly supervene, bacteria invade the walls of the bowel and gangrene to ensue. This process involves the entering and returning portions, but seldom the sheath. The gravity of the conditions provoked by intussusception is determined by the extent of the circulatory disturbance produced by the traction and compression of the vessels of the engaged portion of the mesentery. Mere invagination of the bowel need not lead of necessity either to strangulation of the involved part or to complete obstruction of the lumen of the intestine. But the usual sequence is venous stasis, exudation, infection, inflammation, and finally, gangrene. Chronic cases may give prolonged histories of recurrent attacks of colicky pains in the abdomen, rather vague in character and of irregular occurrence. These are occasionally accompanied by nausea, and rarely by vomiting. During attacks of pain a palpable mass may or may not be present in the right lower quadrant.

*Diagnosis.*—The differential diagnosis is extremely difficult with the exception of those cases in which a palpable tumor is present. In the latter instance the sudden appearance of an abdominal tumor, usually in the right lower quadrant, in association with the symptoms of intestinal obstruction, should suggest the possibility of intussusception, but can by no means be considered as diagnostic. Other conditions, notably large bowel malignancy, may present a similar picture. Those cases, acute or chronic, not associated with the presence of a tumor mass are not to be differentiated, for the most part, from any of the other causes of intestinal obstruction. The diagnosis, then, is chiefly made at the operating table.

The treatment of the condition is always operative and should always include excision of the tumor. This should be undertaken, first, to prevent the possibility of recurrence, and, secondly, to avoid the danger of malignant degeneration. That this latter possibility is not entirely remote is borne out by Collier who states that in 1911 five cases of malignancy of the small

bowel were reported from The Mayo Clinic, of which two started as adenomata with intussusception.

Excision may be effected either by enterotomy and removal or by resection of the gut. The type of procedure adopted is, to a great extent, dependent upon the condition of the involved portion of the bowel. In those cases in which the condition of the gut is good and the intussusception easily reducible, the intestine may be opened and the tumor removed. When, however, the intussusception is not easily reducible or the intestine is markedly inflamed, resection is the safest procedure. The latter may be performed in one stage or, as in the present instance, in two stages.

REPORT OF CASE.—S. S., a white male taxi-driver, aged forty-nine, was admitted to the Jewish Hospital of Brooklyn in February, 1930, complaining of cramp-like circum-umbilical pains, nausea and almost complete obstipation of one week's duration. Patient had taken several enemata without result. Ten years previously he had had an appendectomy and gastric operation for ulcer, the type of operation was unknown. The day previous to admission his pains became more severe and he vomited a black-colored vomitus on several occasions. Shortly after admission he vomited foul, faecal-smelling material. On physical examination, he presented a picture of profound shock. He was extremely pallid and peaked and appeared in *extremis*. General physical examination was negative with the exception of the abdomen. The latter presented a right lower rectus and left upper rectus scar and was not distended. Tenderness was present all over the abdomen and was most marked in the right lower quadrant where marked rebound tenderness was present. Temperature was 101.4°, pulse 120. Blood-pressure was 88/70, white blood cells 15,400 with 86 per cent. polymorphonuclear cells. The urine contained a faint trace of albumen with many hyaline and granular casts.

In view of the patient's precarious condition, no extensive operative procedure was contemplated. That he was suffering from an acute intestinal obstruction was obvious; he presented a scaphoid abdomen, faecal vomiting, was almost pulseless; nevertheless his poor condition demanded an emergency procedure. The origin of the obstruction was believed to be traceable to adhesions from his previous laparotomies. The left upper abdomen was opened through a very small incision measuring about 2½ inches in length, parallel to the rib margin, the first distended loop of jejunum secured, and a Senn (Fig. 1) jejunostomy performed with marsupialization of the bowel to the parietal peritoneum. A large quantity of free serous fluid was noted in the abdomen. One hour after the operation the patient showed marvelous improvement. He felt better. Pulse was of good quality. There was no vomiting or nausea. Post-operatively as well as pre-operatively the patient was given large quantities of saline by hypodermoclysis and intravenously. He drained rather profusely through the jejunostomy tube, retained moderate quantities of food by mouth and had occasional small bowel movements and passed flatus. His cramp-like abdominal pains persisted, however, at first less severe but gradually increasing in severity. Twelve days post-operatively the abdomen was opened again, through a lower mid-line incision. The small intestine was markedly distended and there was found a large intussusception of the ileum through the ileocaecal valve into the caecum and ascending colon, involving about 25 centimetres of intestine. The intussusception was easily reduced by slowly milking out the intussusceptum in the accepted manner. The ileum was found to be almost black, markedly inflamed, cedematous, lustreless, and showed evidence of beginning gangrene. A few inches from the ileocaecal valve was felt a firm mass (Fig. 2) inside the lumen of the ileum close to the apex of the intussusception. The ileum with the encircling mass was brought outside the abdominal wall and a first-stage Miculicz

INTUSSUSCEPTION WITH ADENOMA OF ILEUM

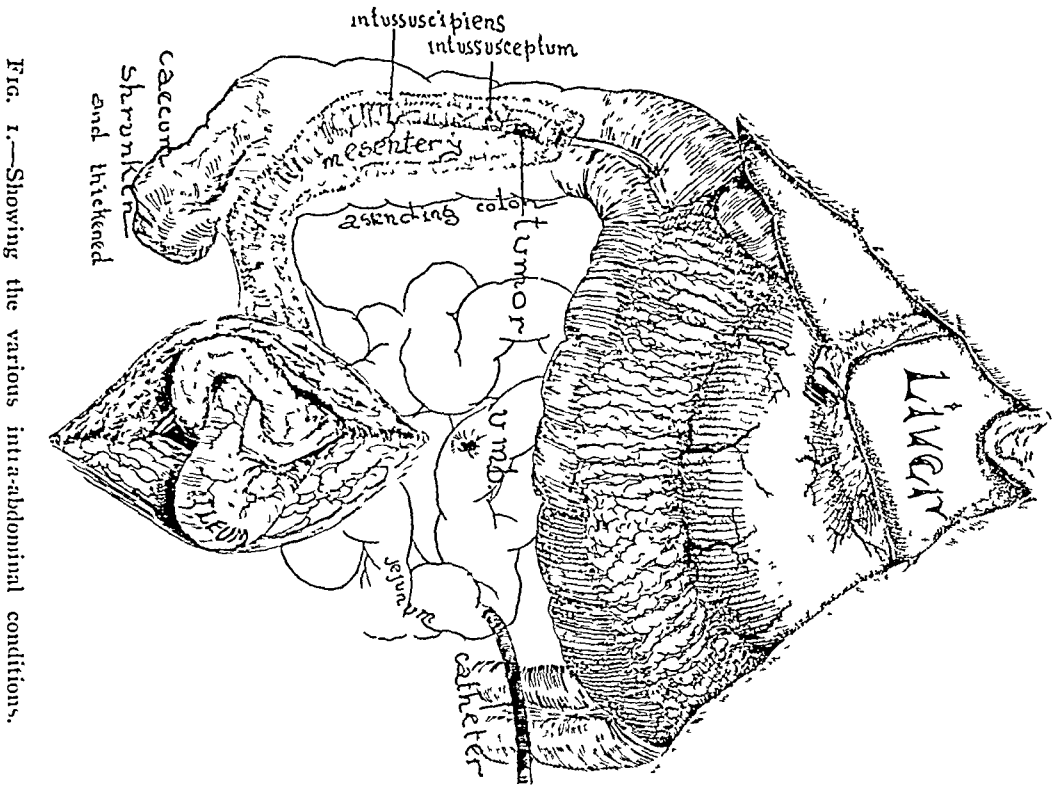


FIG. 1.—Showing the various intra-abdominal conditions.

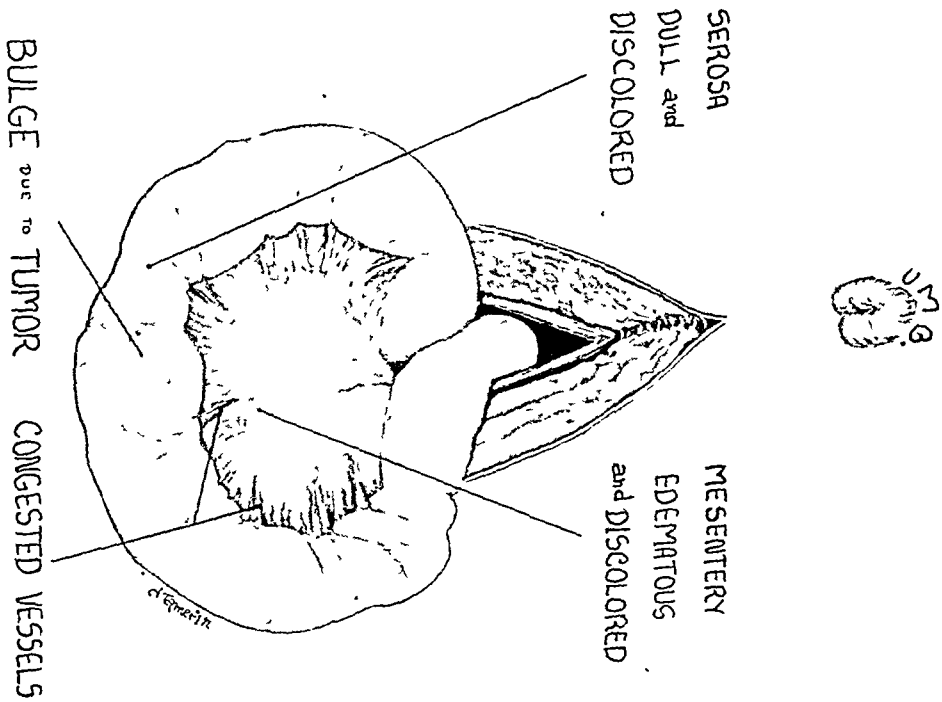


FIG. 2.—Showing the relations of the tumor in ileum.



operation performed. In this case an artificial anus was established through the small bowel. Due consideration and thought were given to the resultant liquid continuous faecal discharge and possible progressive malnutrition. However, the patient's condition, together with the pathological findings, required heroic yet unorthodox measures. Though trite to remark, "the end justified the means." Drainage through the previous jejunostomy was maintained through a catheter. Three days later, that portion of ileum which had previously been brought outside the abdomen was resected to within a short distance from the abdominal wall by cautery. Nine days later a spur clamp was applied in the usual manner and twenty-five days following the first stage the continuity of the ileum was reestablished. The post-operative course was entirely uneventful. Three days after the final closure the patient had his first normal bowel movement, and two weeks following, was discharged.

The resected intestine was 19 centimetres in length. On opening the lumen there was found at the site noted at operation a cauliflower growth within the lumen of the gut about 4 centimetres in diameter, attached to the intestinal wall by a short pedicle. About 2 centimetres proximal to this was found a second polypoid mass about 3 centimetres in diameter with a smooth surface, discolored and red. This growth could not be felt at the time of operation. (Figs. 1 and 2.)

The surrounding intestine was quite oedematous. Microscopical examination showed the intestinal mucosa to be the seat of a localized area of hyperplasia of the glands from which there extended a mass of mucoid substance in which were found strands of deep-staining epithelial cells, distorted in outline. Although the superficial portion of the nodule showed no tendency to alveolar arrangement of the epithelial cells, the portion adjacent to the adjoining normal mucosa was definitely adenomatous in character. There was an associated polynuclear cell and mononuclear cell infiltration with numerous plasma cells found at the base of the nodule in the surrounding intestinal wall. The oedema was limited to the superficial portion of the mucosa. The pathologist's diagnosis was benign adenomatous polyp with mucoid degeneration.

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# JEJUNAL ALIMENTATION

AN EXPERIMENTAL STUDY IN DOGS

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THE matter of feeding human beings and experimental animals solely by bowel has received some attention in recent years from an experimental as well as a clinical standpoint. Clinically the problem is met with in a number of different conditions. The duodenal tube is not infrequently called upon to provide a means of eliminating the stomach for various reasons from its usual rôle in the digestive processes. With recent advances in the surgery of the intestinal tract, surgeons have been called upon repeatedly to perform jejunostomies and ileostomies for divers causes. Most attempts, however, to maintain life satisfactorily under these conditions have not met with success. Duodenal feeding in the hands of the internist has undoubtedly been most successful when employed for short periods of time, *i.e.*, a few days to a few weeks at most (Einhorn,<sup>1</sup> Friedenwald,<sup>2</sup> Friedenwald and Ruhräh,<sup>3</sup> and Lehman and Gibson<sup>4</sup>). The greatest difficulty seems to lie in the fact that it is hard to find a bland food, non-irritating to the gut, which contains enough calories to meet the everyday requirements of the body and enough liquids to maintain the normal hydration state of the tissues, without over-distending the bowel, causing pain, or upsetting the normal digestive processes, producing nausea, vomiting or diarrhoea. In the experimental field this subject of intestinal alimentation has come up recently owing to the efforts that have been made to solve the problem of intestinal obstruction. A number of workers have produced intestinal fistulæ with obstructions of the gut at a higher level in order to feed the animals and thereby eliminate inanition and dehydration as etiological factors in the lethal issue of intestinal stasis (Jenkins,<sup>5</sup> White and Fender<sup>6</sup>). All endeavors in this field, however, have met with only moderate success. No one, as far as we can determine, has been able to maintain life satisfactorily in human beings, or experimental animals solely by jejunal feedings. One of us (A.C.I.) has attempted to maintain dogs solely by jejunal fistula alimentation several times during the past twelve years without success.

Theoretically any method of jejunal alimentation should consider the following physiological principles: First, a bland, non-irritating, easily digested pabulum containing all the essential food elements should be used, and second, it should be administered slowly, simulating the manner of emptying of the stomach. It might be thought that the pabulum should be predigested with gastric juice and have pancreatin and glucose added. We have used

this latter theoretical principle, but have found that such a mixture was irritating to the bowel.

With the above principles in mind, we decided to study this problem with persistence, believing that its solution would be of definite clinical, as well as experimental, value. Dogs were selected for the work because in the first place the physiology of the gastro-intestinal tract of the dog is quite similar to that of man and secondly this animal is the one most commonly used in the study of intestinal obstruction.

In order to have an easily accessible means of introducing the food directly into the bowel, the dogs were first operated. A jejunal fistula was made in the following manner.<sup>7</sup> Under ether anaesthesia and with sterile technic, a right rectus incision was made. The peritoneum was opened and the distal ileum located. A segment of the ileum, about 10 to 12 centimetres in length, and about the same distance from the ileocaecal valve was sought out and isolated by sectioning. The continuity of the ileum was reestablished by an end-to-end anastomosis and the distal end of the segment was then connected to the jejunum about 15 centimetres distal to the ligament of Treitz, by an end-to-side anastomosis. The proximal end of the segment was brought out through a right rectus stab wound. The abdomen was then closed in the usual manner. (The type of jejunostomy generally performed in man does not work well in the dog because of excessive leakage.)

After recovery from the operation each dog was fed in the usual manner on regular dog food until he had fully regained his pre-operative strength and weight and all evidence of abdominal tenderness had subsided. Then all foods and liquids were immediately and completely cut off by mouth. Various diets were then introduced into the bowel in an attempt to find one which would be satisfactory. After trying a great number, one was finally found which would apparently maintain a dog alive indefinitely in an excellent state of health. On this diet two dogs were kept alive one month each during the hottest part of July and August when the afternoon temperature varied between 86° and 103° F. These dogs lost no weight and one even gained slightly. All weights were taken in the morning after a twelve-hour fast. Both dogs were at no time dehydrated as determined clinically by the skin turgor test. They both exhibited unbounded energy and appeared to be in as good spirits, if not better, than the rest of the dogs kept in the same room, fed in the normal manner, on regular dog food.

| <i>Ingredients</i>  | <i>Amount</i>      | <i>Calories</i> |
|---|--------------------|-----------------|
| Water .....   | 3000 cc.           |                 |
| Cane sugar .....  | 150 gms.           | 615             |
| Peptone (dried) .....   | 100 gms.           | 410             |
| Wheat flour .....   | 300 gms.           | 1091            |
| Milk, whole .....   | 2000 cc.           | 1432            |
| Cream, 20 per cent.....   | 1000 cc.           | 1800            |
| Total   | 6550 cc. (approx.) | 5348 (approx.)  |
| $5348 \times 100 = 80.0$ calories per 100 cubic centimetres of food, approximately. |                    |                 |
| 6550  |                    |                 |

## JEJUNAL ALIMENTATION

The diet finally adopted consisted of the following ingredients: Flour, water, cane sugar, milk, cream and peptone. It was usually made up in six-litre lots as shown in table above.

Each 100 cubic centimetres of this food contains protein, carbohydrates and fat in the following amounts: Protein, 3.50 grams; carbohydrate, 8.10 grams; fat, 4.30 grams. The pH of the mixture is approximately 6.0.

Experimentation showed that a dog under our experimental conditions requires approximately 100 cubic centimetres of liquid per kilo of body weight and about 80 calories. Therefore this diet was found ideal, since each 100 cubic centimetres of the pabulum will supply approximately 80 calories. Since the caloric requirements of the dog are more nearly those of the human infant, we feel that an adult will require less than this amount per kilo. But this will have to be determined in each case by the clinician who uses it. Additional water is added to the pabulum to take care of the thirst requirements.

The amount of cream added to the mixture must be varied to meet the alimentary tolerance. Too much cream or fat causes diarrhoea. If any tendency in this direction is observed, the amount of cream is decreased. It may be increased to augment the caloric content of the mixture, if the intestine will tolerate it. Unemulsified fat, such as butter, is to be avoided. Twenty or thirty grams of butter or cod-liver oil will cause diarrhoea in our dogs, unless it is emulsified in bile prior to introduction into the intestine. We have been unable to substitute glucose for the cane sugar, because of the marked tendency of glucose to cause diarrhoea in these dogs. However, if the food mixture is given slowly and continuously, small quantities of glucose are tolerated.

Sufficient sodium chloride is added to maintain the chloride balance of the body, which obviously will vary in different cases. In this dog which has been losing all the gastric juice secreted, we must add 6-10 grams of sodium chloride per day to the pabulum to maintain the balance. We shall point out in a subsequent paper that too much sodium chloride is as bad for such an animal as too little.

The method of making up the food, which is important, is as follows: One hundred and fifty grams of sugar are dissolved in 3 litres of warm water. To this are added 100 grams of peptone (Armour). After both the sugar and peptone have been thoroughly dissolved in the water, the solution is heated to 60° C. for several minutes in order to prevent the milk to be added later from forming large curds. This heated solution is then gradually added to the flour, a paste being first made, and then gradually all the peptone-sugar solution is added. The three litres of whole milk and cream are then added and the entire mixture is brought to a boil quickly over a hot flame, but not allowed to boil. The mixture must be stirred vigorously and continuously while heating to prevent burning. It is kept at a sub-boiling point until it thickens to the desired consistency, which is that of a thick cream soup or thin flour paste mixture. The mixture is then cooled and placed in the ice-box. If kept at ice-box temperature, the food will keep in

good condition four or five days at least. No putrefaction or other changes can be noted in the food at the end of this time.

In feeding, the food is measured out and warmed to body temperature and given through a rubber tube connected to a pressure bottle.

At first the food has to be given slowly and in small amounts, *i.e.*, 200 cubic centimetres are given at one feeding and approximately 30 or 40 minutes are taken to introduce the food. After about a week's time the gut apparently dilates or accommodates itself to this mode of feeding, so that gradually the amount can be increased over a period of one, two or three weeks until quantities as great as 500 or 600 cubic centimetres can be given in a one-hour period. Thus a 10- to 15-kilo dog can be maintained on three feedings a day. However, no matter how easily a dog may accommodate large feedings, it has been found that smaller feedings at more frequent intervals can be digested and absorbed more readily, with less danger of producing diarrhoea. The same methods are adopted in giving the food to humans, and the same cautions must be observed. We believe it more advisable to give it by the Murphy drip method to humans. But only two or three hundred cubic centimetres of the pabulum should be put in the Murphy apparatus at one time, in order to reduce bacterial growth and decomposition, which produce irritating substances. The funnel method that is usually employed is not advisable because too large quantities are introduced in a short period of time cause distress and may lead to peristaltic rushes which will move the food into the colon.

Since this diet is deficient in vitamins, we add to the daily feedings vitamins in the following forms: 10 cubic centimetres of cod-liver oil emulsified in bile; 2-5 drops of viosterol; one egg-yolk; vitamin B concentrate (Harris) 1 gram; yeast "foam," 0.5 gram (fresh moist yeast caused diarrhoea); 0.5 cubic centimetres carotin extract; 20 cubic centimetres neutralized tomato juice. Raw undiluted and unneutralized fruit juices cannot be introduced since they are irritating, *e.g.*, the juice of half a lemon added to a feeding caused peristaltic rushes and diarrhoea in one dog on several occasions.

When not taking food by mouth, the mouth becomes foul and tartar collects on the teeth. This is prevented by washing the teeth daily with dilute lemon juice.

At the time of this writing three patients have been carried along on this pabulum for varying periods with success (one case reported by Dr. Frederick Christopher, in press). We now have a dog that has been maintained on this method of jejunal alimentation for six months in spite of the fact that throughout this period he has lost *via* gastrostomy all the gastric juice secreted, which has averaged 500 cubic centimetres per day. This dog has not only received no food or water by mouth, but has also obtained no fluids subcutaneously, intravenously, or by rectum. All fluids and food have been given solely by the jejunal fistula. This dog has required about 50 cubic centimetres of water per kilo daily to make up for the fluids lost in the gastric juice (10-kilo dog) in addition to the 100 cubic centimetres of food

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per kilo daily. The chlorides lost in the gastric juice have been replaced by adding sodium chloride to the diet. After the dog had been fed on this diet about three months, a secondary anæmia appeared which we have been apparently controlling by the subcutaneous administration of ferric citrate (grams  $1\frac{1}{2}$ ) every other day. This observation falls in line with the observations of Ivy, Morgan and Farrell<sup>8</sup> on the occasional occurrence of anæmia in totally gastrectomized dogs.

### SUMMARY

After many failures a method and a pabulum for jejunal alimentation in dogs has been found which will maintain body weight for long periods. The constituents and method of preparing the pabulum have been listed and described. The pabulum is non-irritating to the gut and is readily assimilated. Food substances which are irritating to the gut have been pointed out. The pabulum is best tolerated when administered slowly, simulating the rate of gastric evacuation, which prevents distress from overdistention of the jejunum and peristaltic rushes from emptying the pabulum into the colon. We are convinced that the pabulum and method of administration will prove to be of definite clinical value on the basis of the fact that all the recommended food mixtures and methods of administration heretofore used clinically proved unsatisfactory for maintaining jejunostomy dogs.

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## INTRAVENOUS UROGRAPHY\*

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THE year 1930 has seen the introduction into urologic diagnosis of a safe and accurate means whereby an intravenous injection of a drug can be followed by a Röntgen-ray examination of the entire excretory urinary tract. Novel as this method is in its perfection, it, nevertheless, celebrates the silver anniversary of such investigative methods. Twenty-five years ago, a young Hungarian student submitted himself to cystoscopy followed by ureteral catheterization; this in turn was followed by a pelvic injection of a colloidal silver preparation whose action was unknown, and this again was followed by a Röntgen-ray exposure. By this personal experimentation performed by Professor Voelker upon Alexander von Lichtenberg, pyelography was born, and from this conjugation of urology with röntgenology, accuracy of renal diagnosis and perfection of renal surgery were enriched one hundred-fold. During these twenty-five years this type of urologic diagnosis has gone through many phases and progressive changes, until we had come to feel that it had reached its perfection, and yet constantly in the background of every worker has been a feeling of insecurity, a lurking sense of danger, and from an inability to describe the normal, there existed an appreciable difficulty of interpreting the pathologic. These evidences undoubtedly suggested to each one working in this field the realization of the value that an intravenous method would give, and though numerous efforts were made in this direction in several clinics, nothing of a tangible and useful character was developed.

*History.*—Professor Arthur Binz, of the Kaiser Wilhelm Institute, Berlin, Germany, had been devoting the greater part of his efforts in recent years to a study of the selectan series of drugs. In this series he had synthetized over seventy preparations and when it was found that some of these preparations had distinct renal affinity, it was debated whether or not, because of their chemical composition, they likewise might not have radiographic value. After several months of abortive effort, in the hands of various investigators, the problem was brought to the attention of Professor von Lichtenberg, of St. Hedwig's Krankenhaus, Berlin. Between them (Professors Binz and von Lichtenberg), there were chosen, out of this series, eleven drugs whose chemical composition suggested the possibility of their being of value in urography, and Doctor Swick, working under Professor von Lichtenberg's direction, first studied their clinical properties.

It is interesting in retrospect to realize that the drug then known as Number 9 was thought at first to be the least likely agent, as its solubility was unusually low and its iodine content low. But, nevertheless, as the work

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progressed, it proved to be the less toxic and the most stable, and is now before us under the name "uroselectan."\*

*Properties.*—Uroselectan has most extraordinary and interesting characteristics. It is a pyridine-iodine compound containing 42 per cent. of organically bound iodine. This chemical compound is stable, non-toxic, non-irritating, and after injection into the body makes its transit and its exit unchanged. Likewise, it does not manifest any irritation when small quantities are injected into the tissues, or if given by mouth or per rectum. The drug is easily recognized and it is simple to estimate it quantitatively. All these characteristics assume greater interest when one realizes that with the administration of the normal dosage, which consists of 40 grams in 100 cubic centimetres of sterile distilled water, there are administered 17 grams of iodine. Investigation has shown that after the injection, the drug will be found in the blood-stream for a period of four hours. A prolonged retention in itself will indicate an abnormal elimination, so that the estimation of it can be utilized as a *retention test of kidney function*. Likewise, investigation has shown that it passes through the kidney by glomerular activity and that 85 per cent. of the drug can be recovered from the urine in four hours subsequent to its administration, if the kidney function be normal. In this wise it can therefore be used as a *renal excretory functional test*. Recovery is obtained by simply acidifying the urine with sulphuric acid, which immediately precipitates the drug and its isolation is secured by filtrations.

After intravenous injection the drug is eliminated from the blood-stream and appears in the renal pelvic urine in about a 5 per cent. concentration. This figure seems to be the maximum concentration that the kidney can eliminate. Experiments *in vitro* show that the density of the X-ray shadow of this drug equals that of  $12\frac{1}{2}$  per cent. sodium iodide solution, only when its concentration approaches, or exceeds, 15 per cent. Therefore, one will not obtain, by the use of uroselectan, even in good kidney function, pictures with as clear-cut a shadow as we are used to seeing with instrumental pyelography. Occasionally, in partial ureteral blockage, greater concentration and sharper pyelographic shadows may be obtained, but this will be the exception rather than the rule.

The intensity of the radiographic shadow is an index and a measure of renal function and renal normalcy, and so for the first time in renal diagnosis we are now enabled to read renal function through X-ray interpretation. Along this same line, let it be understood that again for the first time, we are studying the urinary tract as a whole, and where, heretofore, by instrumental pyelography, pictures were taken of single organs, occasionally a bilateral picture, we were, nevertheless, studying individual organs and trying to determine their relation to a pathologic part or whole. Today, with this new method, the entire urinary tract is visualized and we are

\* By action of the Council on Pharmacy of the American Medical Association it will be known in the future as "iopax."



studying the urinary system as a whole and interpreting its dynamics and its physiologic functioning parts, according to whether or not they be normal or pathologic.

As this drug is eliminated through the renal glomerulus, it stands to reason that those lesions, which in any way interfere with glomerular function, will cause a poor excretion of the drug and a poor visualization of the organ. Hence, we find poor or non-visualization in glomerular disease, in pyogenic infection, in tuberculosis and tumor, but may get remarkably good pictures in cases of advanced tubular nephritis. Non-visualization will also occur in destroyed or non-functioning kidneys, in kidneys undergoing temporary inhibition (anuria), and in kidney abscess. Likewise, one must beware of the occurrence of marked diuresis which might so dilute the drug as to give the impression of poor or non-functioning organs.

*Technic.*—The drug is prepared by dissolving 40 grams of uroselectan in 100 cubic centimetres of double distilled water. This is twice filtered and then sterilized by either autoclave or water bath, as any other intravenous solution would be prepared. It is administered by direct intravenous injection and given slowly at body temperature. Ordinarily, two 50-cubic-centimetre syringes are utilized. We have made it a rule that before starting administration, the patient is fluoroscoped in order to be sure that there is an absence of gas in the intestinal tract. It is obvious that with an excess of gas shadows, it is impossible to satisfactorily read pyelograms by this method. In children, the dosage has been decreased, but not to the extent which other drugs are limited. For instance, we have used from 50 to 80 cubic centimetres in twelve-year-old children; have given 20 cubic centimetres to a twenty-two-months-old infant; 23 cubic centimetres to a twenty-three-months-old infant, all without evidence of any trouble.

Immediately following the injection of the drug, the patient appreciates a sensation of flushing over the body which is accompanied by dryness in the throat. These two symptoms are practically constantly present, and are always of transitory duration, and except for them we have not seen, in over two hundred administrations, any other untoward symptoms. We have not seen thrombosis at the site of injection, nor irritation where some of the drug has been inadvertently lost in the tissues. Following its administration our routine has been to take an informative plate in fifteen minutes. This plate should be immediately developed, and if it shows evidence of good elimination, we empty the bladder and take stereoscopic plates forty-five minutes after the injection. These can be read and from them the time interval judged, but, on an average, the final pair of plates are usually taken at an hour and a quarter after injection, and these are taken in the prone and in the erect posture.

If there is evidence of low function, the above time intervals can readily be changed, and if function is particularly depressed, one might not obtain satisfactory elimination and good visualization until hours have passed by,

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as satisfactory pictures have been obtained as long as twenty hours after administration in cases of advanced kidney disease.

One can immediately appreciate the advantages of this method, with its time element so prolonged, when compared with the necessity of rapid work when taking the usual instrumental pyelograms. Early plate reading will frequently give one the suggestion to take the subsequent pictures in varying postures, and one must realize that oftentimes a poor picture may carry the best prognosis.

We have been somewhat spoiled, or at least misguided, by our past experiences with instrumental pyelography, and though the pictures so obtained are evidently more brilliant and sharper in outline than are to be seen with intravenous urography, nevertheless, everyone has appreciated that the pictures have been obtained at a sacrifice of everything that might be termed physiologic. The catheter has been passed retrograde through the ureter, an irritating solution has been injected (too frequently to the point of tolerance), and pictures have been snapped with the patient oftentimes undergoing marked muscle spasm. These factors we have learned somewhat to appreciate, avoid, or discount, and withal we have been obtaining remarkably clear-cut outlines of pelvic topography. But it is because of the clearness of these pictures that it has been the effort of many to try to make intravenous urography duplicate them in the sharpness of detail. Procedures, such as the Trendelenberg position; compression air bags over the lower abdomen; increased dosage of the drug; catheter blocking of the ureters, but when one tried in an effort to improve the visualization of this drug over and above its normal excretory index of 5 per cent., one realizes the uselessness of such measures. In fact, it is by avoiding such artificial means that we can today rid our studies of the artifacts of yesterday. So, let me again accentuate that now, for the first time, we are reading renal function and the dynamics of the urinary tract through a visual portrayal of the entire functioning urinary system, and we are anxious to get an undisturbed physiologic picture and to do away with the artifacts of instrumental pyelography.

*Indications.*—Intravenous urography is indicated: Where cystoscopy fails or is attended with difficulty as: (a) In tuberculosis of the bladder; (b) in vesical hæmorrhage; (c) in urethral stricture; (d) in extensive bladder tumor; (e) for intolerant patients; (f) in active infections; (g) in deformities; (h) in prostatic obstructions; and (i) in infants and children. There is no anæsthetic necessary and there is no age limitation.

Intravenous urography is also indicated in those renal conditions where ureteral catheterization cannot be done, is contra-indicated, or fails, such as: (a) Ureteral obstruction; (b) ureteral malformation; (c) acute or chronic adnexal disease; (d) severe tuberculosis; (e) rectal implantations; (f) rupture of the bladder; and (g) rupture of the kidney.

Intravenous urography settles once and for all the question of simultaneous bilateral pyelograms, and becomes a distinct advantage, therefore,

in recognizing the occasional case of polycystic disease, the existence of bilateral hydronephrosis, and the recognition of fused, solitary, or malformed kidneys.

Intravenous urography is particularly valuable in the study of the dynamics of the urinary tract, either as a whole in peripheral obstruction, or in part in ureteral obstruction. It is interesting to feel that we are watching work.

Intravenous urography is of distinct value in studying cases of ureteral calculus, for here we get not only our most brilliant pictures, but it will inform the surgeon of those cases which are in need of immediate operation because of complete blockage of the ureter, and will distinguish these from the cases where only a partial blockage exists, and time might be spent in cystoscopic endeavors to aid the stone's passage.

Intravenous urography has already taught us certain physiologic functions which until now were unknown. It has proved the existence of a diastole and systole of the renal pelvis. It has disproved the contention that the renal pelvis is normally emptied and has shown that it is normally almost completely filled. It has given us new ideas in regard to the normal anatomy and location of the ureter, an organ which, heretofore, has been depicted, but only under abnormal conditions. It has taught us to appreciate the peristaltic wave of the ureter, and to interpret the normal from the abnormal; it has shown us characteristic narrowing and isolated dilatations, and has put the subject of ureteral stricture where it belongs.

*Contraindications.*—Investigation has shown that though the major portion of uroselectan is eliminated through the kidneys, a small portion is excreted through the liver, and at the same time the skin seems to act as a depository for the drug in smaller quantities. While high-grade kidney deficiency may not be a contraindication to the administration of the drug, it becomes one as it is useless to expect any pictorial results if kidney function is markedly depreciated. If, in addition to renal disease, there exists hepatic disease, the administration of the drug is considered contraindicated. In cases where poor results are obtained, one must not only think of deficient function, but must likewise realize that active elimination may be playing its part. This, however, is easily excluded, or included, for a well-outlined bladder shadow will immediately indicate good function even if the upper urinary tract shadows are absent; while a poor vesical shadow will immediately prove deficient function on the part of the kidneys. Whenever there is doubt, one must realize that this is but one method of investigation and that the older procedures of cystoscopy, of ureteral catheterization, of the study of separated specimens, of the differential function tests, and of instrumental pyelograms are not to be neglected and are often quite definitely indicated in aiding the interpretation in a difficult renal study.

#### CONCLUSIONS

1. Pyelography by uroselectan is an entirely physiologic procedure and outlines the entire urinary tract devoid of artifacts, giving simultaneous

functional reactions, and permitting the study of the dynamics of a whole system.

2. Good pictures are neither expected nor actually wanted, for we are reading renal function to be surgically interpreted, and do not want, or need, artificial accentuation. As a visual portrayal of renal function, outstanding pictures indicate abnormalities, and this is especially true in ureterograms as characteristically observed in ureteral obstructions.

3. Failure of excretion indicates lack of unilateral or bilateral function, and here the cystographic outline from the drug's elimination is the key to the renal activity.

4. Problems of interpretation will naturally and constantly arise, but we will learn to overcome them and experience will eliminate them all in time. One should not hesitate to fall back upon the more tried and understood methods of ureteral catheterization, differential function tests and instrumental pyelography, but the most important and most valuable adjunct of this method will be the establishment of a close coöperation between the röntgenologist on the physical side, and the urologist on the clinical side, and unless this coöperation is sought for and forthcoming, there is danger that this method, so easy of administration, and so difficult of interpretation, may lead to two unsuspected errors: one, that needless surgery will be undertaken on insufficient grounds; and second, that early diagnosis and necessary surgery will be denied from inadequate interpretation.

## PRIMARY CARCINOMA OF THE OVIDUCT

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A LESION which occurs in about 0.45 per cent. of all genital tumors, that, out of 250 reported cases, has in but one instance been diagnosed before operation, and which, in addition, is associated with only 0.45 per cent. three-year cures, should be carefully studied whenever possible.

We present, in this report, the only case on record in the Gynecological and Pathological Departments of the School of Medicine, University of Louisville, of primary oviduct carcinoma, and wish, also, to summarize briefly some of the preceding excellent reviews of the literature on the subject.

*History.*—Renaud,<sup>1</sup> in 1847, recorded the first primary carcinoma of the oviduct, but not until 1888 did Orthmann<sup>2</sup> give the first complete description of the lesion. Barth and Sanger,<sup>3</sup> 1895, gave the first detailed description and classification, which has remained classical to date.

Since then there have been reviews of the literature. The most outstanding of these are Vest,<sup>4</sup> 1914, Wechsler,<sup>5</sup> 1926, Laing,<sup>6</sup> 1927, Whorton and Kroch,<sup>7</sup> 1929, and with the latter publication the number of recorded cases was brought to 232. The literature has been so thoroughly covered by the above authors that we wish but to enumerate those cases that have been published since the article of Whorton and Kroch, and add the one case from our laboratory. Eighteen cases have been reported, distributed as follows: Wolf,<sup>9</sup> 1, 1928; Scott and Oliver,<sup>12</sup> 2, 1929; Callahan,<sup>13</sup> 1, 1929; Bortini,<sup>15</sup> 1, 1929; Watkins and Wilson,<sup>8</sup> 1, 1930; Stanca,<sup>14</sup> 1, 1929; Cowan,<sup>16</sup> 1, 1930; Anspach,<sup>10</sup> 2, 1930; Holland,<sup>11</sup> 8, 1930.

In recent years there has been a rapid rise in the number of reports in this country, indicating that more careful attention is being given the disease, and that there is a more accurate reporting of cases.

*Etiology.*—The etiological factor is as yet undetermined. *Sterility* is not more common in women with carcinoma of the tubes than in women with other pelvic tumors. Thirty-two per cent. in Wechsler's cases were sterile, and 29 per cent. had only one child. The number affected with pelvic inflammatory disease will explain some of these cases of sterility.

Chronic salpingitis was present in only 8 per cent. of Wechsler's cases. Is it not possible that in some cases the infection may be secondary to the papillary growth? If chronic salpingitis is a predisposition toward cancer, it is also a help in developing a barrier against early dissemination by sealing off the tube, thus aiding in the closure of lymphatic channels by inflammatory reaction and scar tissue formation.

## CARCINOMA OF THE OVIDUCT

One group of authors believe that foetal anlage or embryonic remnants are predisposing factors. The tubes and the uterus arise from the muellerian ducts. The epithelium of the uterus, however, undergoes tremendous changes during menstruation and pregnancy and is exposed to infection and traumata more frequently than the tubal mucosa. The tubal mucosa is all of one type, inactive to a great extent, and well protected in most instances, changing but little during menstruation and pregnancy. There is only one point where a transition of mucous membranes occurs, namely at the cornu of the uterus, where primary papillary carcinomas are rarely, if ever, found. So it seems that some of the so-called predisposing agents in the production of carcinoma do not often exist in the tubes, which may be one of the determining factors in its rarity.

There is, however, a sequence of associated changes in the genital organs which may be of significance. In 74 per cent. of the cases reported, the disease occurs after the patient's fortieth year; in 27 per cent. of instances, cystic changes in the ovaries are associated with it; and in about 17 per cent., fibroid changes in the uterus. In senility we think of changes in the cellular structure as toward atrophy and fibrosis. But with premature senility, and especially in the presence of infection in tissues that have a papillomatous arrangement, could not this early senile change be that of stimulation and abnormal undifferentiated growth, rather than atrophy and fibrosis? In other words, growth is excited before the phase of degeneration appears, and a susceptible individual, under these conditions, might develop carcinoma.

*Symptoms.*—There are no essentially characteristic symptoms and their duration varies from a period of months to years, at times blending with symptoms of pelvic inflammatory disease and fibroids. Cancer of the oviduct is more rapid in growth than cancer of the fundus, but not so rapid as ovarian cancer.

The earliest and most constant symptom of primary carcinoma of the Fallopian tube is pain located in iliac regions, usually definite and severe, sometimes sharp and colicky, or cramp-like and paroxysmal, and a profuse amount of discharge from the vagina. In view of the frequent association of the disease with uterine fibroids, the sharp pains may be superimposed upon a long-standing, dull pelvic ache.

Vaginal discharge may be of the most variable character, from serous watery discharge to blood-tinged, with varying degrees of color, due to the degeneration and oxidation processes in the blood, during its passage into the vagina. The amount of discharge is also variable and may be spasmodic.

The menses are commonly disturbed and almost every type of menstrual irregularity has been observed. Metorrhagia and menorrhagia are most common, and are associated at times with a foul odor. The menstrual disorders are so varied and inconsistent as to be of little aid in the diagnosis.

Weakness and weight loss are found in about 25 per cent. of cases. Gastro-intestinal symptoms, genito-urinary symptoms, backache, and other

symptoms are no more frequent in this disorder than in other pelvic conditions, so they, too, are of little help in the diagnosis.

The rarity of tubal carcinoma, together with the absence of any characteristic signs or symptoms, makes the diagnosis very difficult.

If a woman at or beyond her menopause develops a blood-tinged or serous watery vaginal discharge associated, or not, with rather severe persistent pain, and by bimanual examination the uterus is not found enlarged, but an adnexal mass is felt, with or without a known cause for the mass, and if curettage reveals no pathology of the endometrium, tubal carcinoma should be suspected, and laparotomy advised.

Indiscriminate use of radium to arrest vaginal bleeding, without a definite diagnosis, has been one of the causes of delay in the treatment of some of these cases.

It is a wise precaution, when operating on pelvic inflammatory cases which are in the cancer age, to have available a pathologist who will open the oviducts and examine them before the abdomen is closed. If a papillomatous mass is found, a radical operation may be done immediately, if the patient's condition warrants.

*Treatment and Prognosis.*—The consensus of opinion is that the best form of treatment is block dissection of both oviducts, ovaries and uterus in early cases, with a wide dissection of broad ligaments and parametrial areas. In cases where there is a question of metastasis a thorough radiation of the abdomen should be given after primary healing.

. Due to the variable and incomplete procedures of the past, and the late stages of the growth when found by the surgeons, only about 04.5 per cent. of the cases reported have obtained a three-year cure of the disease.

The causes of such a high mortality in these cases are due to:

(1) Highly malignant growth. (a) Peritoneal implantations early. (b) Rapid metastasis by means of broad ligaments and lymphatics. (2) Retardation in diagnosis and overlooking early unsuspected cases. (3) Incomplete surgical procedures. (4) Cases with questionable metastasis not followed up with radiation. (5) Insufficient diagnostic criteria to detect early cases.

*CASE HISTORY.*—E. S., aged forty, colored, was admitted to the Gynecological Department of the Louisville City Hospital, June 10, 1930, with a diagnosis of uterine fibroids and salpingitis, her chief complaint being pain in lower left side of abdomen, abdominal tumor. Her family history was essentially negative. She had had two full-term pregnancies, no miscarriages; otherwise her personal history was also essentially negative. Menses began at thirteen years of age, regular, every thirty days, duration three days; after first pregnancy, twenty-three years ago, has had a prolongation of periods to five days, with slight whitish discharge and dull pelvic pain. Condition has otherwise remained the same.

*Present Illness.*—April, 1930, menstrual period was more painful than usual; about three weeks later, May 25, 1930, bleeding began and this period was associated with much pelvic pain, no clots in flow; vaginal discharge remained the same and vaginal bleeding continued until June 16, 1930, date of operation. About the beginning of the last period of bleeding, May 25, patient noticed a rather sharp persistent pain in lower, left quadrant of abdomen and during past week has had nocturia one to two times,

## CARCINOMA OF THE OVIDUCT

increasing weakness, and dizzy, swimming sensation in head. Bowels regulated. Has not noticed loss in weight. She was a well-developed and nourished colored woman of forty years of age. General examination was essentially negative, lungs clear to percussion and auscultation, pulse 90, blood-pressure 156/90. Her abdomen was rounded and rather thick-walled; on palpation, a rather firm tumor mass which extended almost to the umbilicus was made out; inguinal glands palpable, no definite localized tenderness. There was some bloody vaginal discharge, no Bartholin glands palpable. The cervix uteri was enlarged, firm, lacerated; the pelvis was partially filled with a firm, irregular tender mass, with most marked tenderness on the left side. There was also some tenderness on right, but size of pelvic mass and tenderness did not permit detailed adnexal examination.

June 16, 1930, she was subjected to supravaginal hysterectomy, bilateral salpingectomy, left oöphorectomy, appendectomy. Uneventful convalescence; patient discharged from hospital at end of three weeks. The wound healing had been *per primam*; general condition good.

*Pathological Findings.—Gross Description.*—Specimen consists of body and fundus



FIG. 1.—Low power to show the invasion of the tube on all sides and filling the lumen.

FIG. 2.—Low power to show the arrangement of the tumor growth in imperfect glands and papillary processes

uteri, with attached tumor masses, oviducts, left ovary and the appendix. Attached to the uterus are numerous tumor masses, some of which are subserous, others are intramucous and one is submucous. The largest measures 11 centimetres in diameter and the smallest ones are barely visible. These tumors are light pink in color, are very firm and on section reveal interlacing striæ quite typical of leiomyomata. The uterine cavity is made irregular by the submucous tumor and it is also distorted by traction from other tumors in the wall. The mucosa is not remarkable.

The distal portion of the left oviduct is expanded into a bulbous mass, measuring 40 by 22 millimetres and the end is sealed. It is soft, but not fluctuant. Section reveals the enlargement to be the result of grayish, friable tumor growth entirely filling the lumen and extending deep into the wall (Fig. 1). Small portions of it are yellowish in color and evidently necrotic. The ovary is attached. It is about one-half normal size and sectioned surface reveals a number of follicular cysts in various stages of development. The right oviduct is not remarkable. The entire mass weighs 1500 grams. The appendix measures 90 by 3 millimetres. The distal portion is almost embedded in the mesenteric fat. There is some scar tissue extending from appendix down into mesentery for a short distance. Cross section reveals no lumen, the central portion being light-colored, firm scar tissue.



*Microscopical.*—The lumen of the appendix is filled in by old scar tissue in which there are a few lymphocytes. There is some scarring also in the outer coat. The lesion is entirely healed.

Sections of the uterine tumor masses reveal a smooth muscle parenchyma with a moderate amount of connective tissue stroma, in which hyaline degeneration has begun. The cells are all well formed and regular in size, shape and staining reaction. Sections of the uterine wall reveal a very slight, diffuse lymphocytic infiltration throughout the musculature. There is early hyaline degeneration of the connective tissue and these nuclei are pyknotic. In the mucosa there are a few lymphocytes also. Glands are few; there is some œdema.

*Oviduct.*—Sections of the left tube show the central portion to be made up of neoplastic tissue composed of epithelial parenchyma and new connective-tissue stroma (Fig. 2). The epithelial cells are elongated and are otherwise similar to those of the mucosa of the oviduct. They are arranged in a few imperfect gland formations, but for the most part in papillomatous forms with a varying amount of connective-tissue stroma. Deep in the wall there are quite a number of irregular solid masses of epithelium

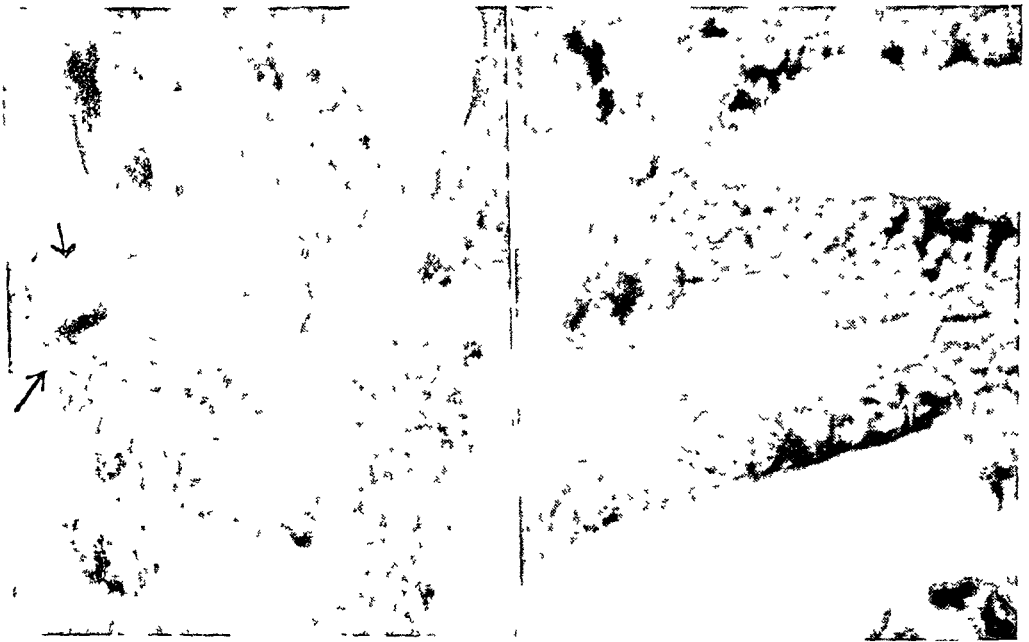


FIG 3—High power to show the type cell which is columnar and also the atypical cells. There is one mitosis in the central left portion.

in which the cells are quite irregular in size, shape and staining reaction. Some of them are multinucleated. Mitoses are moderate in number and among these there are many atypical mitoses (Fig. 3). Deep in the wall the tumor is forming very little stroma of its own, using the wall of the tube for its support and nourishment. The tumor does not extend deep into the broad ligament, nor does it extend into the ovary.

Sections of the ovary show the Graafian follicles to be in various stages of development, but arrested. The lining epithelium is degenerating.

*Microscopic Diagnosis.*—Leiomyomata of uterus; chronic metritis, slight, with hyaline degeneration; retention follicular cysts of ovary; carcinoma of the oviduct, adeno type.

Three types of carcinoma of the uterine tube have been described. One is a papillary type of epithelial growth, the structure of which is very similar to the normal tubal mucosa. In the second type of growth the epithelium is

## CARCINOMA OF THE OVIDUCT

arranged in imperfect gland-like structures. It has been suggested that possibly these are formed by fusion of the adjacent papillæ, but very probably they are copies of the deeper part of the mucosa, where the epithelium is arranged in gland-like forms. A third type is made up of a squamous-like epithelial cell, very probably resulting from metaplasia of the normal epithelium. In these tumors there is cornification and pearl formation.

In carcinomas of the oviduct, like neoplasms elsewhere, there are mixtures of different types of structure; the most common being a mixture of the first two types, which we might call a papillary adenocarcinoma. The case here reported falls into this group.

It has been suggested that these tumors might have their origin in an accessory tube or in Gartner's duct, or from the uterine mucosa, or from the ovary. Any of these structures might give us a similar tumor. Obviously, however, only the malignant neoplasms arising from the mucosa of the uterine tube should be included in this group.

### CONCLUSIONS

(1) Oviduct tumors, although rare, are associated with only 4.5 per cent. three-year cures.

(2) The diagnosis is still dependent upon the macroscopic and microscopic examination.

(3) Careful study and reporting of all cases of primary oviduct carcinoma should be done, so as to develop criteria for earlier diagnosis.

(4) Cases of vaginal bleeding, and oviduct tumors when operated upon should be subjected to quick pathological examination before the abdominal closure, then early cases may be found and more complete operations performed.

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# CARCINOMA OF THE CERVICAL STUMP FOLLOWING SUBTOTAL HYSTERECTOMY\*

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AND

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MANY opinions have been expressed as to the method or methods which should be used to avoid development of carcinoma of the cervical stump following supravaginal or subtotal hysterectomy. Leonard<sup>3</sup> gave credit to Chrobak<sup>2</sup> as the first to call attention to the possibility of malignancy developing in the cervical stump following supravaginal hysterectomy. Since his time many cases have been reported in the literature, particularly in Germany, France, and this country.

Although statistics differ as to the frequency of occurrence of carcinoma of the stump of the cervix, depending on the country from which they come, we find, too, that percentages differ within the different countries. The error of figures is most likely to occur in the individual interpretation of what constitutes subtotal, or supravaginal hysterectomy. If one surgeon performs direct amputation above the cervix that is one consideration; if the next surgeon in addition cones or cups out the cervix and its lining mucous membrane, that is another consideration.

There are reasons other than statistical misinformation why, in some countries, the cervix is of vital concern; in others, not. European countries have more control medically over more people. The tears and lacerations of childbirth are less neglected; this is in contrast to Hawaii, where almost every city block has its midwife and the hospital rarely shelters the obstetrical patient. It is in localities of the latter type that virulent malignancy of the cervix is an endemic problem.

From an etiologic standpoint efforts have been made to associate carcinoma of the cervix with uterine fibromyomas. Leonard<sup>3</sup> stated that 3 per cent. of all fibromyomas of the uterus are associated with carcinoma of the cervix. Few hold to this viewpoint. Among others, Tesauro,<sup>9</sup> in 1928, reported ten cases from Faure's clinic, in which carcinoma of the cervix developed after subtotal hysterectomy, and in only four of the ten had the primary operation been done for fibromyoma of the uterus. Trauma and irritation form at least part of the etiologic picture of malignancy in this region, and those facts must be kept in mind when the choice of surgical procedures is under consideration.

Polak<sup>6</sup> quoted the combined experience of Schlottleander, Spencer and Nobel which involved 900 cases. Total hysterectomy had been done for

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\* Read before the Southern Surgical Association, December 9, 1930.

clinically benign conditions, and the cervix was later examined pathologically. In 2 per cent. of these cases carcinoma of the cervix was found. Sharples<sup>7</sup> also quoted this percentage.

If we must recognize the possibility of carcinoma being present in the cervix and being overlooked in 2 per cent. of the cases in which subtotal hysterectomy is performed, the proponents of preferential hysterectomy already have a platform to stand on. Further review of reported cases adds to its support.

Tesauro<sup>9</sup> reported the time interval in his cases between subtotal hysterectomy and development of recognized carcinoma of the stump of the cervix at nineteen, fifteen, twelve, eleven, nine, eight, seven and three years, and in one case as ten months. One of his cases is worthy of particular mention. Subtotal hysterectomy had been done fifteen years previously for retroversion and salpingitis; then an ulcer of the cervix developed for which radium was used. One and a half years later operation was performed because of recurrence of the ulcer, and histologic examination revealed carcinoma of the cervix at the level of the cervical lymph nodes. Immediate recurrence of the carcinoma followed operation. In one case at the clinic, carcinoma developed twenty-nine years after subtotal hysterectomy had been performed.

Leonard,<sup>3</sup> Stein<sup>8</sup> and many others reported cases with a history of a long interval between the primary operation and the occurrence of carcinoma in the stump. All of this adds to the proof that even though malignancy is not present in the cervix at the time of operation the likelihood of its development is ever present if the cervix is left intact.

We present further evidence as to the truth of the foregoing contention. A review of the cases in our clinic reveals that between January 1, 1910, and July 1, 1930, ninety-nine patients presented themselves with carcinoma of the cervical stump following subtotal hysterectomy. A consideration of these patients as a group disclosed certain interesting facts: Following hysterectomy performed at the clinic, cervical carcinoma developed in twelve cases in which the operation was performed for benign conditions, and in three cases in which it was performed for questionably benign conditions. Following hysterectomy performed elsewhere, cervical carcinoma developed in twenty-three cases in which the operation was performed for benign conditions, and in sixty-one cases in which it was performed for questionably benign conditions.

The low incidence of carcinoma of the stump of the cervix in cases in which subtotal hysterectomy was done at the clinic may be attributed to the frequency with which, for many years, the technic of cupping or coning out the cervix from above has been employed, thus removing all of the cervical canal.

The time of diagnosis of carcinoma of the stump of the cervix after subtotal hysterectomy may be noted in Fig. 1. A larger number of cases of carcinoma of the cervical stump is found within the first two consecutive

## CANCER RECURRENCE IN CERVICAL STUMP

years after subtotal hysterectomy than in any two years thereafter, although more than 50 per cent. occur three years or more after subtotal hysterectomy; the condition is serious because ultimately so few patients are cured.

Relative to the treatment in cases of carcinoma of the cervical stump, it must be recalled that prior to 1915 little advance had been made therapeutically with Röntgen-rays and radium. Of our group of ninety-nine cases it will be advisable to operate for the carcinoma in nineteen; in seven of these hysterectomy had been performed in the clinic, and in twelve it had been performed elsewhere. Radium was given in eighty-four cases and treatment by Röntgen-rays in seventy-eight cases, after the method as outlined under the modified grouping of Bowing and Fricke.<sup>1</sup>

Since it is the purpose of the surgeon to restore health and to insure, so far as he is able, the future health of his patient, it behooves him to consider seriously the potentialities of the cervical stump when he is confronted

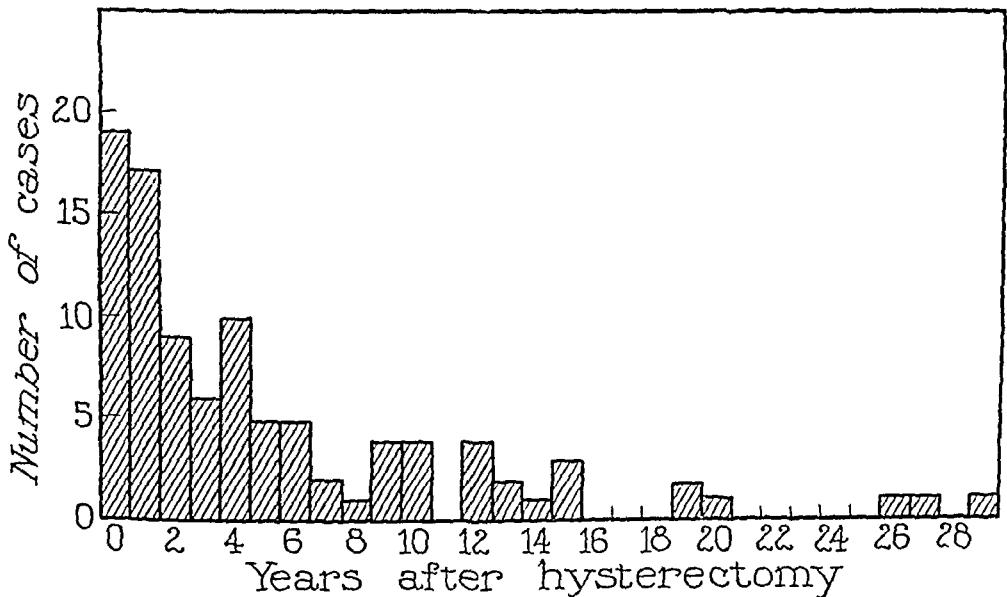


FIG. 1.—Time of diagnosis of carcinoma of cervix after subtotal hysterectomy for benign condition.

with the problem of total *versus* subtotal hysterectomy. Uniform technic is no more possible than uniform mortality, and difference of opinion is as healthy as it is at times annoying. However, regardless of views to the contrary, Masson<sup>4</sup> has shown that it is possible to perform total hysterectomy with mortality as low as, or lower than, that following subtotal operations; he now performs the subtotal operation in less than 10 per cent. of the cases. When subtotal hysterectomy is the procedure of choice, it is well to adopt, if possible, the added technic of cupping or coning out the cervix to the vagina, particularly if the women have borne children or if there is any suspicion that foci of infection are present.<sup>5</sup> It is appreciated that the degenerating, non-resistant cervix may possibly become a chronic focus of infection, resulting in an apparently new disease at some distant point. The cervical tissue may at any time become malignant.

Carcinoma developing in the remaining cervix is usually not diagnosed until the disease is far advanced, and although treatment may prolong life.

cure is rarely obtained. Certain surgeons maintain that total abdominal hysterectomy is more dangerous than subtotal abdominal hysterectomy. Perhaps this opinion arises partly because the surgeon elects to carry out total abdominal hysterectomy in the more serious type of case.

To check this point we have compared the hospital death rate following 3,085 subtotal abdominal hysterectomies with that of 1,588 of total abdominal hysterectomies, which were performed for fibromyomas of the uterus at our clinic in the years 1916 to 1929 inclusive. We included only fibromyomas in both series in order to make them comparable with respect to surgical risk. The death rate in the series of subtotal abdominal hysterectomy is 1.2 per cent.; that in the series of total abdominal hysterectomy is 1.8 per cent. This difference of 0.06 per cent. in the death rates is so small that it could arise by sampling, nine times in a hundred.

From these facts we conclude that the difference in death rate between total abdominal hysterectomy and subtotal abdominal hysterectomy is very slight, if any, and that the higher death rate usually attributed to total abdominal hysterectomy is probably due to the selection of graver surgical risks, rather than differences due to operative technic.

It is also claimed that more patients would die from the complete operation than would die from carcinoma developing in the remaining stump of the cervix. If surgeons who fear to perform total hysterectomy accept the responsibility for the future life and health of the patient, and feel that the cervix is a potential source of carcinoma and often an area of focal infection, we would suggest that they perform subtotal hysterectomy, and follow this procedure ten or twelve days later by some method of removal of the cervix, enucleation of the canal, or destruction of the cervical canal by cautery. Occasionally this procedure brings to light otherwise hidden early carcinoma, as may be noted in the 900 cases reported by Polak. This procedure would not increase the mortality, and would accomplish all that is desired. The patient who has had subtotal hysterectomy alone should be advised to return from time to time for observation. In some cases it may be advisable to use the actual cautery on the cervical stump or prophylactic douches in an attempt to clear up infection.

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# THE TREATMENT OF GAS GANGRENE

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FROM the fact that by far the greatest part of our knowledge of gas gangrene has been dearly won in the ghastly operating rooms of war hospitals, the impression has gained ground that this infection is a relatively infrequent occurrence in the general practice of surgery. Though of course not so common as during the war, reports in the literature indicate that the disease is not so rare in civil practice as we are wont to believe. It is a fairly common complication of so-called "street accidents." It has been described as occurring after simple tonsillectomy, during labor, following abdominal operation, after amputation of the extremities, and even occasionally after hypodermic injections. To the surgeon whose patient has developed this condition after a crushing street accident, the outlook may be sad enough; but to one "who has stood a helpless spectator" while his patient has succumbed to a gas infection following a common surgical procedure, the situation must appear tragic in the extreme.

Several years ago while on the service of the late Doctor Brickner, I had the opportunity of observing and treating a small number of street-accident cases which developed gas gangrene. In spite of repeated amputations at succeeding higher levels, in spite of the use of perfringens serum, the only kind then available, all of our patients died. Within recent years at the Hospital for Joint Diseases, several patients whose legs were amputated for diabetic or arteriosclerotic gangrene, and one whose gall-bladder was removed for acute gangrenous cholecystitis developed a gas infection and despite all efforts, died, while the surgeon stood almost impotently by "watching the disease develop under his eye and almost under his hand."

In one of the following two cases even despite the use of anti-gas gangrene serum the fatal outcome was not avoided.

CASE I.—M. T., male, aged fifty-two, was first seen September 3, 1930, with a history of sudden pain in the calf of the left leg. There was a history of diabetes over a period of twelve years. This had been kept more or less under control by moderate dietary regulations. When first seen there was a black discoloration of the left big toe and several smaller areas of bluish discoloration on the dorsum of the left foot. Neither the dorsalis pedis nor the posterior arteries could be palpated. There was a marked amount of sugar in the urine, and the patient was advised hospitalization. On September 5, 1930, Doctor Ringer admitted the patient to his service and the following data were determined: blood-pressure 112/70; white blood cells 8,700; 62 per cent. polymorphonuclears; hæmoglobin 80 per cent.; temperature 99.6° F., pulse 104, respiration 84; blood sugar showed 210 milligrams per 100 cubic centimetres of blood. The popliteal and the femoral arteries were easily palpable. The patient was promptly put on a rigid anti-diabetic regimen with the use of insulin, so that by September 14, the urine

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showed no sugar and no albumin, and the blood sugar had been brought down to 100 milligrams per 100 cubic centimetres. In spite of all these measures along with conservative treatment of the ulcerating areas, the discoloration appeared to be spreading, due to progressive reduction of the arterial supply. September 24, though the leg and thigh appeared to be normal in color, pulsation, though still present in the external iliac, could not be felt in the femoral artery. September 29, Doctor Ringer notified Doctor Kleinberg that in his opinion an amputation should be done. At this time the external iliac pulsation could not be well felt. A mid-thigh amputation under ethylene, carbon dioxide and oxygen anæsthesia was performed September 30 without the use of a tourniquet. Two large rubber dam drains were inserted and the wound was closed with interrupted stitches. The patient left the operating room in good condition. The pathologist reported a marked narrowing without complete closure of the external iliac and the femoral arteries. On section, "the lesion was found to be an endarteritis, the intima of the vessels is extremely thickened, the changes are not those observed in gangrenous gangrene, nor are they those of thrombo-angiitis obliterans. The changes are due to early sclerotic endarteritic occlusion of the vessels." Following operation, the blood sugar rose to 100 milligrams per 100 cubic centimetres of blood, and the temperature gradually rose until it reached 105° F. just before death October 3, 1930. On October 2, the urine showed 3½ per cent. sugar, acetone 3 plus, diacetic 3 plus. Insulin was given. Because of the rise in temperature and the poor condition of the patient, the wound was inspected. It was "found dry and clean. There are no evidences of gangrenous areas and no crepitation under the skin." In spite of the usual cardiac stimulation, and intravenous glucose injections, the patient gradually failed and died at 5:30 on the morning of October 3rd. An autopsy performed five hours later disclosed marked icteric discoloration of the skin. "No evidence of suppurative infection at the site of the amputation. On opening the stitches, a necrotic hæmorrhagic appearance is observed in the muscles, associated with definite crepitation of the subcutaneous tissues of the thigh. The thigh is swollen and the swelling extends to the lower portion of the abdomen. On making the abdominal incision the subcutaneous tissues of the abdomen were found congested and œdematous." Subsequent report of the cultural examination of the pus taken at the time of the autopsy showed the presence of *Bacillus welchii*.

CASE II.—L. K., male, aged sixty-three, was admitted to the service of Doctor Brickner March 25, 1930, with a diagnosis of acute cholecystitis. There was a history of seven days' abdominal pain which began in the right upper quadrant, and which was associated with nausea but no vomiting. The pain continued to grow worse and radiated to the back. For the past two nights he had slight chills. The right upper rectus was found rigid, but could be relaxed under gentle pressure. There were slightly roughened breathing, dulness and a few crepitant râles at the right base posteriorly. The blood-pressure was 165/65. The temperature was 101.6° F., the pulse 110, respiration 32. In spite of a marked glycosuria, immediate laparotomy was deemed necessary in the face of an acute abdominal emergency. The operation was performed under spinal anæsthesia. A pericholecystic abscess and a tensely distended gall-bladder with several necrotic areas in its wall were found. The abscess was cultured. To avoid unnecessary manipulation, drains were inserted into the gall-bladder and into the abscess without removal of the gall-bladder. The patient left the operating room in very good condition. On the 26th and 27th he appeared to be making satisfactory progress with a slow drop in temperature and pulse. Late in the afternoon of the 27th the temperature rose to 100.6° F. and the next morning the patient was found disoriented with a temperature of 101.8° F. The blood count had risen to 19,400 with 80 per cent. polymorphonuclears. Examination of the blood showed 429 milligrams of sugar per 100 cubic centimetres. Inspection of the wound disclosed a widespread, subcutaneous emphysema over the whole right half of the abdomen down to the symphysis. The patient immediately was ordered to the operating room. Under local anæsthesia three longitudinal incisions

were made in the abdominal wall and the necrotic portions of the right rectus muscle were resected. The wound was packed with hydrogen peroxide gauze and left wide open. 100 cubic centimetres of anti-gas gangrene serum was given intravenously. In spite of vigorous stimulation, glucose intravenously, hypodermoclyses and meticulous irrigation of the wounds with hydrogen peroxide, the patient continued to grow worse. The following day all of the longitudinal incisions were connected by cross incisions and the whole abdominal wall laid wide open. The right rectus was entirely necrotic. Parts of the muscle were turbid, yellowish in color, solid in consistency, contained no gas bubbles and looked like boiled meat. Other parts were red-brown in color, flabby in consistency, and contained gas. Culture of the abscess was reported as showing typical staphylococcus aureus and *Bacillus welchii*. The interstitial connective tissue was permeated by a foamy, sanguinous fluid. The necrotic parts were excised, the wound repeatedly flushed with potassium permanganate and the wound dakinized. The condition of the patient grew steadily worse and early in the evening he died. At autopsy, four hours later, the whole process appeared to be localized to the abdominal incision while the peritoneal cavity appeared relatively clean.

In cases such as those reported above the need is urgent and the outcome is precarious to the last degree. What is to be done? How can the disease be cured once it has developed? Are there any means by which it may be prevented in cases where experience teaches it may be expected to show itself?

Before proceeding to a consideration of the means which have been used in the treatment of this dread infection we may be permitted to pause a moment for the emphasis of two important facts. In the first place, not all infections which give evidence of gas formation are by that token alone to be considered as gas gangrene. I recall a case in which an explosive evacuation of gas followed the incision of a huge abscess of both ischio-rectal fossæ though no evidence of gas bacillus was found and the aged, debilitated patient made a prompt recovery following simple drainage. Landsman<sup>1</sup> reported a similar case in which only "the usual pus-forming organisms" were found while McKittrick and Pratt<sup>2</sup> observed that in diabetic gangrene "the production of gas by ordinary pyogenic organisms is a disturbing complication." In the second place the mere demonstration of the gas bacillus in a wound culture is not conclusive evidence that the patient has or is about to develop gas gangrene. During the course of an amputation of one of our fatal cases, I myself have been stabbed without any consequence, by a needle which had just penetrated severely infected muscle tissue. Macrea<sup>3</sup> noted that he had "seen the gas bacillus (*welchii*) injected into healthy muscle of the normal arm with no effect whatsoever." Neither of these criteria can be looked upon as specifically indicating the presence of the syndrome of gas gangrene.

Gas gangrene is a local, progressive affection of contused and lacerated muscle tissue which is characterized by a severe systemic toxæmia, and is not to be looked upon as a specific entity but rather as a clinical picture resulting from the symbiotic effects of anaërobic and aërobic organisms introduced into wounds. In war injuries or street accidents the appearance of these organisms can be fairly well explained. In abdominal wall infections

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occurring after operations on the intestinal tract or its appendages, the presence of these bacteria may be predicated on contamination from the intestinal contents, their normal habitat. But, their occurrence in amputation stumps even where no previous ulceration had existed is somewhat difficult to understand. By some, the development of infection under such circumstances has been attributed to the use of infected instruments, or of catgut containing viable spores. Except for the fortuitous discovery of such infected catgut in routine examinations before operation, this explanation is seldom available in any individual case since the infected material is buried deep in the wound. By others, the belief has been expressed that the disease develops secondarily to gas infection in a gangrenous area or even as a result of contamination from the skin. A third possibility, that the bacteria may be dormant in apparently healthy muscle until activated by the trauma incident to the amputation must be considered. In this regard the following two cases may be of some interest.

CASE III.—D. H., male, aged seventy-four, was admitted to the service of Doctor Kleinberg October 7, 1930, complaining of pain in the third right toe. Eight months ago the toenail had been removed at one of the city hospitals and thereafter the toe became swollen. Wet dressings were applied for six weeks with but slight improvement of the condition. In June of 1930, the patient was treated at the Hospital for Ruptured and Crippled without any improvement. When admitted to our hospital in October, 1930, the patient's general condition was unsatisfactory. The terminal half of the middle toe was gangrenous and the foot was swollen. No pulsation was felt in the dorsalis pedis or posterior tibial artery. The blood-pressure was 140/78, temperature 99.6° F., pulse 80, respiration 20. October 10 under local anæsthesia the toe was amputated and the wound was closed with interrupted stitches without drainage. During the next twelve days, the patient appeared to be doing well. The temperature and pulse were normal and the general condition was excellent though he still complained of great pain in the toe. Examination indicated pus in the depths of the wound which was consequently opened and dakinization begun. From this time until December 9 regular dakinization of the wound was carried out. On December 9 the following note was made: "The general condition has not improved, the wound has been dakinized and is smaller and cleaner, but there is a purplish discoloration of the second toe which probably means impending gangrene." For several weeks mid-thigh amputation had been urged but he refused to consent until December 12, when under spinal anæsthesia and without the use of a tourniquet a long-posterior-flap amputation was performed at the junction of the middle and upper thirds of the thigh. The wound was drained and closed with interrupted stitches. The pathological report of the specimen showed "arterio-sclerotic gangrene with intimal thickening of the vessel and medial calcification." The following day the patient had a moderate rise of temperature and on December 14, the temperature rose to 105.° F. The wound smelt of hydrogen sulphide though no gas crepitus could be felt. At 10:15 all sutures were removed and the wound irrigated with hydrogen peroxide. Both culture and smear were sent to the laboratory and reported subsequently as showing gas bacillus (*welchii*). At 1 P.M. the skin of the posterior flap was found dusky and some crepitation was found on the front of the thigh. There was a strong odor of hydrogen sulphide from the wound which was consequently widely opened. The tissues in the depths were found necrotic and grayish in color. The wound was irrigated with hydrogen peroxide and the patient ordered to the operating room. Under nitrous oxide anæsthesia three vertical incisions were made in the thigh. The wounds were left wide open after being washed

repeatedly with hydrogen peroxide and Dakin's solution. Two hundred cubic centimetres of polyvalent serum were injected intravenously and the wound exposed to the Quartz lamp. In spite of the usual stimulation and post-operative treatment, the patient gradually failed and died at 9:15 P.M. No autopsy was permitted.

CASE IV.—M. Q., female, aged fifty-six, was admitted to the service of Dr. H. C. Frauenthal June 18, 1930, with the following history. In August, 1929, she had been treated at the hospital for an osteomyelitis of the first left metatarsal. A hallux valgus operation was performed on the right side, and the head of the first left metatarsal amputated. In September, 1929, there was marked improvement. In November, 1929, she had a corn removed beneath the fifth right metatarsal. The wound did not heal and the foot became markedly swollen and painful. Wet dressings were applied for five or six weeks with subsidence of the acute symptoms, but healing did not supervene. Some five or six weeks thereafter a small operation which was not described was performed on her right foot since when her foot had become progressively worse. When admitted to the hospital her temperature was 100.6° F., pulse 96, respiration 20. There was found on the postero-lateral aspect of the fifth metatarsal, two small sinuses from one of which a seropurulent discharge issued. The skin was red and excoriated over two-thirds of the dorsum of the foot. Over the internal malleolus there were small necrotic areas. The urine showed a faint trace of albumin and 3 per cent. sugar. The blood showed white blood cells 14,000, 79 per cent. polymorphonuclears, and 294 milligrams of sugar per 100 cubic centimetres. The patient was put under stern diabetic control and the foot was treated conservatively with heat, wet dressings, etc. The temperature however, continued gradually to rise to its highest point, 105.4° F. On July 8 marked gangrene of the foot was observed and a mid-thigh amputation was advised, which was done on the following day under spinal anaesthesia. The pathologist reported "medial calcification with thrombus formation and recanalization." The day following operation the temperature dropped and the general condition of the patient appeared much better, but thereafter the temperature again began to rise so that on July 15, it was 102.4° F. On this day the wound was inspected. Though no discharge or redness was noted, the edge of the wound was found puckered. "The appearance of the wound would lead one to believe that this cannot be responsible for the temperature. Sutures to be removed nevertheless." July 26, inspection of the wound showed the presence of maggots. A foul odor, thin coffee-ground pus, gangrene of the skin and slight gas crepitation were observed. The wound was thereupon cultured and promptly dakinized. July 29, the condition was found much the same though the maggots were fewer in number. The patient was in severe shock, but this was thought to be due to an insulin hypoglycæmia. Wound culture performed this day was subsequently reported as showing streptococci and *B. coli* but no *Welch bacillus*. The following day culture of the wound showed *B. coli* only but many Gram-negative bacilli were seen on the smear. On the 31st, gas crepitation was noted on the posterior part of the thigh as far as the gluteal fold, and the posterior flap was found gangrenous. On this day the patient died, and culture of the pus showed *B. welchii*. Blood culture was reported on August 3 as sterile. Autopsy disclosed a gas bacillus infection along with signs of generalized arteriosclerosis.

The long latent interval before the development of gas gangrene in these two cases may perhaps justify the suspicion that the organisms may have remained dormant in the tissues of the thigh until the conditions for their growth became propitious. On the other hand it must be admitted that in the first of these two cases, which was pre-operatively prepared in a routine manner by the hospital attendants, the possibility of skin contamination, as, for example, after giving an enema, must be considered. In the second case the possibility that the contamination was secondary to maggot infesta-

tion, must also be held in mind. Still, if these are valid explanations, one should expect the presence of similar infections in other equally extensive wounds throughout the hospital. That this has not occurred would seem to indicate the mediation of other factors. It is considerations of this sort which led to the suggestion that anaërobic organisms might possibly find a site of predilection in poorly oxygenated tissues such as are to be expected in the type of patient here described.

That gas bacilli may be found in the tissues of patients who had suffered from previously contaminated wounds is a known fact. The question as to whether these organisms, transported either by the blood or lymphatic streams, may be found in tissues not previously subjected to such contamination is of vital importance since it may establish an important prophylactic indication. In studying 216 slaughtered hogs, Reith<sup>4</sup> found that of 77 per cent. of these animals which showed bacteria latent in their muscles 37 per cent. contained bipolar anaërobic rods. A somewhat similar condition was found in live hogs, guinea pigs and rabbits. Ford<sup>5</sup> also concluded as the result of a study of normal organisms in different animals, (a) that each species of animal showed a microbic growth peculiar to itself, (b) that each animal preserved its own organism, and (c) that each organ preserved its own bacteriological flora. That organisms may be transported through the blood stream without the clinical signs of sepsis has been demonstrated by studies on the bacterial excretion of the kidneys. May it not be true that human tissues have also their normal bacterial content or that under special circumstances, such as impaired circulation, presumably sterile tissues may become the locus minoris resistentiæ in which organisms normally present in the body may localize. To determine this point, cultural studies of the gangrenous areas as well as of the tissues at the site of amputation are at present being undertaken in the laboratories of the hospital, primarily on patients subjected to operation for arterial disease.

In the past, practically every known antiseptic solution has been advocated in the specific chemotherapy of this disease; iodine, iodoform, Labarraque's solution, nitrate of silver, hypochloride of soda, soap, flavine, rivanol, dichloramine, ether, alcohol, formol, etc. All have been disappointing, either because it was found that when strong enough to be really bactericidal these solutions caused death of tissue and so predisposed to spread of the infection, or when weak enough to be non-injurious to tissues they were practically useless as antibacterial agents. Thereupon the discontinuous use of antiseptic solutions such as Dakin's solution was suggested but with similarly unsatisfactory results. It was felt that though this solution was beneficent as a bactericide and as a mechanical detergent, it was disadvantageous in that, at the same time, it flushed away the protective antibodies and leucocytes.

In an effort to combat gas infection on a biological basis, potassium permanganate, oxygen and hydrogen peroxide were used in the hope of oxygenating the tissues and of thus rendering them unsuitable for the growth of anaërobic bacteria. The results appeared to have been no better

than those obtained with other agents. Indeed Delbet<sup>6</sup> showed experimentally that the gas bacillus grew better on muscle tissue previously treated with hydrogen peroxide than on muscles not so treated. As a result of Taylor's demonstration of the bactericidal effect *in vitro* of 1 per cent. solution of quinine sulphate on the gas bacillus, Pilcher<sup>7</sup> suggested a quinine mixture which was employed with considerable satisfaction both by him and others, though it does not appear to have received general approval. Sir Almroth Wright proposed the use of hypertonic saline solution in dressings, and Delbet<sup>8</sup> because of its positive chemotaxis for leucocytes recommended a solution of 1.21 per cent. magnesium chloride. Phototherapy, heliotherapy, and thermotherapy have all been used with but the same indifferent success. Though of auxiliary value in the treatment of the disease, no one nor any combination of these agents can be considered as invaluable in a case of impending or progressing gangrene. The only apparently certain means at our disposal are surgical and serotherapeutic.

In an earlier contribution<sup>9</sup> on the subject of the surgical treatment of gas gangrene, it was observed that "all cases of gas gangrene are serious and unless promptly treated they are almost always fatal. The prognosis depends to a great extent on the character of the infecting organisms. Those cases in which streptococci are found in symbiosis with the anaërobes present a decidedly worse prognosis than those in which only anaërobic bacteria are cultured. In the superficial, or localized types of the disease, it may be possible by prompt surgical treatment to save the affected limb. In the more virulent, diffuse types, the sacrifice of the limb may be considered a small price to pay for saving a life."

Whether, in a case of injury, wound excision (*épluchage*) should be performed prophylactically to prevent "contamination" from becoming "infection" (of any kind) will be decided by the surgeon according to the nature of the injury, the structures involved and the probable character of the contamination. When there is crushing or other necrosis of tissue it is certainly wise to excise devitalized skin, fascia and muscle, and to evacuate blood from the wound, as a means of reducing the probability of infection especially by anaërobes.

If any suspicion of gas gangrene arises there should be prompt *débridement*, *i.e.*, free incision through skin and muscle sheaths to release tension, to afford drainage, to evacuate gas if present, and to admit air to the tissues. If the muscle shows characteristic brick-red (in later stage greenish) color, swelling and lack of contractility, it should be submitted to free *épluchage*—either excising through normally red and moist muscle that contracts lively under the knife, or removing the entire muscle or muscle groups (according to Blake and others), as may be needed. The extirpation must be bold, and through uninfected tissue.

In the diffuse, rapidly spreading type of gas gangrene, prompt amputation preferably circular, and, certainly, without suture of the stump, well above the zone of infection is, if possible, unfortunately indicated. Whether

after débridement, épluchage or amputation, particular care must be taken to permit free access of air to the wound. Gauze packing is dangerous, in that it excludes air and causes a damming of the wound discharge, and thus encourages spread of the infection.

Beyond this type of mutilating surgery our mainstay must be the therapeutic use of serum. During the early stages of the war in France, individual sera were prepared against the *bacillus bellonensis*, *perfringens* and the *vibrio septique*. As in the case of the *perfringens* serum prepared by Bull, all proved failures and the reason was not far to see; the individual antisera produced for one type of organism were quite powerless to affect the growth of the other organisms found in gas infected wounds as shown by Weinberg and Seguin.<sup>10</sup> Following this, polyvalent sera were proposed by Weinberg and Seguin, Leclainche and Vallee, and by Vincent and Stodel. Though the polyvalent serum did not appear to be specific in the cure of the disease, a prompt dropping in the mortality was noted. Weinberg and Seguin reported nineteen cures in thirty cases. Lardennois and Baumel<sup>11</sup> used the sera of Leclainche and Vallee, of Vincent and Stodel, and of Weinberg and Seguin. They concluded the last chapter ("Serotherapy") of their monograph on gas gangrene with the statement, "The response to serotherapy is rapid. Four or five hours after injections the patient revives, becomes reanimated, arouses from torpor; the pulse rapid, and scarcely perceptible becomes slower and stronger; the dyspnoea diminished, color returns in the face; it is truly a resurrection. Locally, swelling subsides and the tissues become more supple; the odor lessens and the gaseous infiltration decreases."

In this country until relatively recently a polyvalent serum was not obtainable and the results obtained from the use of the simple *perfringens* serum were for the most part unsatisfactory. Where the polyvalent serum has been used, as by Larsen and Pulford<sup>12</sup> and in the case herewith reported, the results have been eminently satisfactory.

CASE V.—G. S., female, aged thirty, was admitted to the service of Doctor Brickner October 12, 1929, after having suffered a severe laceration of the left arm in an automobile accident. The patient was immediately given tetanus antitoxin and transported to the operating room where an avulsion of the brachioradialis at its origin and a large lacerated wound almost completely severing the triceps were noted. The head and contaminated tissues were widely excised, the muscles were resutured and the wound was liberally drained and closed with interrupted stitches. Following operation, the temperature slowly began to rise and the patient complained of pain in the axilla and in the chest. On the 14th, the lower flap of skin appeared devitalized, and on the following day the patient complained of more severe pain. There was a foul, brownish discharge around the drain and a few bubbles of gas could be expressed from the wound. The wound was promptly opened widely and irrigated with hydrogen peroxide. Smear taken at this time was shortly reported as containing streptococci, staphylococci and numerous short Gram-positive bacilli which subsequently proved to be *B. welchii*. The patient was promptly removed to the operating room. Free incisions of the skin and fascia were made, necrotic muscle removed and the wound repeatedly flooded with hydrogen peroxide and potassium permanganate 1 to 1000. At the termination of the operation 200 cubic centimetres of polyvalent anti-gas gangrene serum were given intravenously and



four hours later another 100 cubic centimetres. The following day Doctor Brickner noted: "The general condition of the patient is better, the wound is wide open, there is still much swelling at the ends of the triceps but there is no suppuration, no odor or spread of the infection; dakinization started." This prompt and vigorous effort toward control of the gas infection seems to have been eminently successful for on October 20, a note was made to the following effect: "The wound is granulating with some surface suppuration and superficial sloughing. The gas infection appears to be entirely controlled. Wound irrigated with zonite one to four every two hours." Thereafter the patient made an uneventful recovery except for the appearance of a mild attack of erysipelas which developed after an operation for the plastic closure of the huge wound on the back of the arm. On December 14 the patient was discharged, being able to extend her elbow to 170 degrees, and to flex it to 90 degrees.

The serum which Larsen and Pulford used contained 70 units of perfringens antitoxin, 5 to 10,000 of tetanus antitoxin, 62,000 M.L.D. of vibrion antitoxin, and 130,000 of M.L.D. oedematiens antitoxin. It was given intravenously in doses of 50 cubic centimetres of antitoxin in 100 cubic centimetres saline every twenty-four hours, and in addition 50 cubic centimetres of antitoxin were applied locally to the wound. The antitoxin used in our case contained 4,000 units of tetanus antitoxin, 15,000 units of perfringens, 35,000 M.L.D. of vibrion and 20,000 M.L.D. of histolyticus antitoxin per 100 cubic centimetres of saline. A double dose was given directly after operation and another 100 cubic centimetres were given after an interval of four hours until the infection appeared under control. In the other cases in which the same serum was used, the unsuccessful results may have been due to the fact that the serum was not given as persistently as in the above case. On the other hand sight must not be lost of the fact that the conditions in this case and in the others were entirely different. The satisfactory outcome was observed in a relatively healthy young person while the fatal cases occurred in much older persons suffering from arterial diseases as well as diabetes. When the serum is administered early smaller amounts will be necessary than when administered late. The amount to be given and the interval at which it should be given must be determined by the clinical evaluation of the severity of the infection and the patient's response to the treatment.

Though the specificity of this polyvalent antiserum in the cure of definitive gas gangrene is not completely established, there is no doubt of its great value in reducing the mortality when used as a curative measure and in reducing the morbidity when used prophylactically. Indeed its greatest importance may lie in its use as a preventive measure. Lardennois injected 30 cubic centimetres of the polyvalent serum of Leclainche and Vallee or Vincent and Stodel into the injured muscles. He quotes Duval as having observed 381 wounded soldiers, by the nature of their wounds candidates for the development of gas gangrene, who received prophylactic injections and of whom only eighteen developed the disease. Duval is also reported to have had the information that in the German army, among 1,200 wounded soldiers from two divisions, one of which had received prophylactic injections

and one of which had not, the gas gangrene morbidity in the first was 0.3 per cent., while in the second it was 3 per cent. This observation is probably either similar to or identical with that subsequently reported by Rumpel<sup>13</sup> to the effect that in a division which had previously been given prophylactic serum injections, the morbidity dropped to 0.6 per cent. whereas in division not treated, the morbidity remained at 3 per cent. The experience of French surgeons in the use of these polyvalent sera has been so satisfactory that it has been used, apparently with success, both in the treatment and in the prophylaxis of peritoneal infections following appendicitis, pulmonary gangrene, etc. Its use in the former condition is justified both by the results which they report and by the frequency with which bacteriological evidence of gas bacillus has been found in cases of gangrenous appendicitis with peritonitis.

The prophylactic dose of polyvalent gas gangrene antitoxin is now being prepared in conjunction with tetanus antitoxin for commercial sale in this country. It contains 15 units of tetanus antitoxin, 10 units of perfringens, 10 units of vibron antitoxin and is as easily administered as tetanus antitoxin alone. But for its prohibitive cost it should be given in all street-accident cases just as tetanus antitoxin is now routinely administered. In cases of amputation for arterial disease, particularly in the presence of diabetes, it seems as if the preventive dose of polyvalent serum should be given as part of the routine preparation of the patient. If it can reduce the mortality from gas gangrene in anything like the proportion suggested by other writers, it will amply justify its routine use. For the private patient the cost of this dose, about three dollars, can be of no importance if the likelihood of a complication by this disease may be reduced. For the ward patient the serum should be supplied at a nominal cost by municipal laboratories. There is as much justification for the manufacture and distribution of this serum at public cost as there is for the manufacture and distribution of tetanus antitoxin.

In addition to the prophylactic use of sera, it may be important to direct attention to certain other auxiliary means of preventing the development of gas infection. Shock must be energetically combated, and the tendency to acidosis controlled by alkalization both of the local wound and of the patient. Wherever possible, either local, spinal or nitrous oxide gas should be used as the anæsthetic of choice since chloroform and ether tend to the production of acidosis and so favor the development of a gas infection. McKittrick and Pratt found a relatively low percentage of gas infections in their series. It may be concluded from the cases here reported that this infection in diabetics is a complication of the utmost gravity even when the diabetes appears to be under control. In the pre-operative preparation of the patient McKittrick observes, "it has been our policy to assume that such infections (gas) are contaminations of the skin introduced at the time of operation unless there was a demonstrable gas-bacillus infection before operation. For this reason we prefer no pre-operative scrub with soap and

water to one carelessly done and carried too close to the gangrenous areas." In addition to the careful pre-operative preparation of the patient suggested by McKittrick it would appear advisable to insist upon the use of sterile gloves by the person undertaking the preparation so as to avoid any possibility of extraneous contamination. And finally, in cases where anoxæmia of the tissues may be predicated on the basis of a preëxisting arterial disease, the use of a tourniquet, even though it may facilitate the performance of an operation, should be interdicted as tending to further impair the nutrition of the tissues.

From what has gone before, the following inferences may be drawn. In the treatment of the definitive disease radical surgery, even including amputation, and the liberal use of a polyvalent serum are the only dependable measures at hand. In the prevention of the disease the routine use of prophylactic serum should be advocated in all cases of street accidents as well as in the pre-operative preparation of patients suffering from certain afflictions such as arterial disease, diabetes, etc. Shock, acidosis, and diabetes should be energetically combated. Local, spinal, or gas anæsthesia should be chosen in preference to ether or chloroform. The tourniquet should be forbidden even at the inconvenience of the surgeon.

My thanks are gratefully accorded to Doctors Kleinberg, Frauenthal, and Brickner for permission to use their case records.

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# THERAPEUTIC AND PHYSICAL PROPERTIES OF ULTRAVIOLET IRRADIATED PETROLATUM\*

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OF NEW YORK, N. Y.

ABOUT one and one half years ago, my attention was attracted by the fluorescence of petrolatum under the play of the ultraviolet light. This is a property by no means possessed exclusively by petrolatum.

In order to use this fluorescence as an indicator, I placed a quantity of petrolatum in a test tube, corked it and hung it on a curtain where it would be bathed in ultraviolet light. After a time, it occurred to me that I would obtain a more intense fluorescence by using a vita-glass test tube.

I procured a vita-glass test tube and filled it with petrolatum and placed it where it would be bathed in ultraviolet light each time the light was turned on. There was no detectable difference in the fluorescence between the petrolatum in the ordinary glass test tube and that in the vita-glass test tube.

Without any special care as to distance or time of exposure, this tube was exposed in all perhaps two hours.

At that time, I had visiting me a patient whom I had operated upon one year previously, who had what was thought to be a tumor of the ascending colon but which proved to be a chronic appendiceal abscess of long duration. A gangrenous cast of the appendix was removed and the abscess cavity was drained. The wound healed except for a fistulous tract which persisted and defied all efforts at cure for a period of one year. The patient suffered from pulmonary tuberculosis and this was considered a factor in the persistence of the sinus, but microscopic examination of the scrapings did not reveal evidences of tuberculosis.

Before sending him back to the hospital, in order to attempt a surgical closure, after having employed many of the advocated applications, it occurred to me, on the merest chance of success, to fill the sinus with the irradiated petrolatum that had been so long in preparation.

Owing to technical errors, my first two attempts to fill the cavity failed. I improved my technic and the third time I succeeded in filling the entire cavity with the warmed irradiated petrolatum. The wound was covered with gauze held in place with adhesive plaster. I did not see the patient until five days later when he came to see me, with the greeting: "Doctor, I think my wound is closed." His wound was closed and has remained so.

I was much impressed by this sudden reversal of conditions but my years of clinical experience have made me skeptical of generalizing from solitary results.

Since that time, I have had numerous opportunities of using irradiated

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\* Read before the Clinical Society of the Hospital for Joint Diseases, January 6, 1931.

petrolatum in a large variety of wound infections, both primary and post-operative, in chronic sinuses, empyema sinuses, ulcers, burns, tuberculous joints, etc.

In this preliminary report, I shall make no attempt to summarize the clinical details of my cases but I shall merely state in a general way what is seen following its application. In the case, for instance, of an extensive cellulitis in which drainage has been instituted and there is copious purulent discharge, if warmed irradiated petrolatum be applied directly to the wound and covered with gauze and bandage, and left for a day or two, a marked change in the wound and in the exudate will be seen at the next dressing.

The character of the exudate will be found to be much less purulent, the wound itself will be covered with granulations, sloughing will have been aborted and healing will be on its way.

After the second dressing, the wound will be found to be in an advanced state of healing and the infection practically subsided. The character of the discharge will have become serous. The bacterial count will be greatly diminished, or entirely absent.

In the case of a post-operative wound infection which ordinarily would require extensive drainage, a small opening need only be made in the wound in order to permit the escape of the exudate and, by means of a syringe, the warmed irradiated petrolatum is directly injected into the suppurating cavity, filling it entirely. A covering of gauze is finally applied.

I have many times seen such infections subside in twenty-four hours and close completely in four or five days. Chronic empyema sinuses that have remained open for months, I have seen close in two weeks.

Two cases of fistula in ano, that had persisted for years, were each closed after one injection.

A chronic discharging tuberculous sinus of the elbow-joint, after persisting for three years, was cured after twelve injections, covering a period of six weeks.

Sinuses following the drainage of appendiceal abscesses are promptly rendered bacteria-free and completely closed in two to five days following the injection of irradiated petrolatum.

In one case of tenovaginitis of the index finger and palm of the hand in which the culture showed streptococcus hæmolyticus, the incisions were filled with warmed irradiated petrolatum and at the first dressing, thirty-six hours after the operation, not a sign of pus was seen in the wound.

Chronic bone sinuses are very favorably affected by the injection of irradiated petrolatum as are also tuberculous affections of the hip- and knee-joints but the final word cannot yet be expressed in this report.

*The effect of the irradiated petrolatum seems to be dependent upon a strong bactericidal action upon the ordinary organisms of wound infection together with a potent stimulus to the processes of wound healing.*

The bactericidal potency of this agent is amply proven by its clinical action when applied directly to the infected wound; the character of the dis-

charge is speedily changed from a purulent one to a serous one, and the bacterial count diminishes rapidly. The physical properties of the material render the ordinary bacterial studies, as applied to pure cultures in the laboratory, difficult to execute. The stimulating effect upon cellular metabolism is characterized by the rapid production of vigorous granulations followed by an unusually speedy closure of the wound.

As to this newly endowed therapeutic virtue imparted to petrolatum, it appeared to me that it might be due to vitamin D. Being acquainted with the extensive labors of Hess and Steenbock and others, on ultraviolet irradiation, vitamin D appeared to be a satisfactory answer to the question of the causation of this action of irradiated petrolatum. It seemed an easy matter to prove this conclusion by the simple process of injecting viosterol into wounds instead of irradiated petrolatum.

FIG 1.—Shadow of test tube from radiance emanating from luminous string and cord.

This, I then proceeded to do, but no such favorable wound reaction followed as I had seen with irradiated petrolatum. I then mixed equal parts of viosterol and plain petrolatum and applied this mixture to wounds, following which also the prompt cleaning up of the infection failed to appear. I returned to the use of irradiated petrolatum and again obtained prompt disinfection of the wound and healing.

It became evident then that my assumption, that I was getting a vitamin D effect, was erroneous, but wherein lay the virtue of the irradiated product. I did not know. I had frequently observed that after prolonged irradiation of forty minutes or one hour, the petrolatum became considerably darker than before irradiation. Ordinary yellow petrolatum became an orange-brown and white petrolatum became yellow. Liquid petrolatum remained unchanged.

Evidently, irradiation brought about some physical change, perhaps in its molecular arrangement, that caused an optical alteration such as has

been found in crude coal tar oil by Herrick and Sheard,<sup>1</sup> by spectroscopic examination. In the dark room, there was no visible luminosity as might have been anticipated as I was dealing with the invisible part of the spectrum. After fumbling around for a time, it occurred to me to place my vita-glass test tube, filled with irradiated petrolatum and stoppered with a cork with a piece of string on it, upon a photographic film in a light-tight box. This I did and left it for five days. (Fig. 1.) At the end of that time, I developed the film and found that I had obtained a photographic impression but not at all as I might have had reason to expect. Upon studying the film, it became evident that the cork and the string which had become smeared with the petrolatum had become actinically radiant and produced recognizable impressions upon the photographic film. The entire film had been bathed by the radiation, except where the vita-glass tube lay and this had caused a

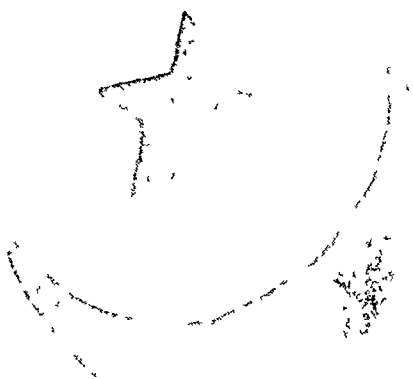


FIG 2.—Photographic impression from irradiated petrolatum

FIG 3.—Photographic impression from petrolatum irradiated through blue glass filter.

wide divergent shadow, protecting the film from a radiance emanating from the cork and string.

I began then to realize that the agent that I was employing was a radiant energy, picked up from the zone of invisible light of the ultraviolet field and that whatever therapeutic virtue I observed must be accredited to this source. I soon learned that the petrolatum became much more actively endowed when directly exposed to the action of the rays, rather than through vita-glass.

A long series of experiments followed in which a method was developed, by means of which I was enabled to compare the actinic value or photometric intensity of my product. By the same means, I tested out a great variety of substances and found that with few exceptions the oleaginous substances took up the secondary radiance. The sugars are absolutely negative as are also the proteids. Among the oleaginous substances that take the actinic value, some hold it longer than others. From the therapeutic standpoint, it was found that most of the vegetable oils contain an acrid acid such as oleic or stearic, which is offensive to the tissues, whereas the mineral oils are bland and inoffensive, even when inspired in a vaporized condition.

The photometric method of estimating the actinic value acquired is as follows: Take a flat receptacle such as a Petri dish and pour into it warmed, irradiated petrolatum so that the bottom of the dish is covered to the thickness of about  $\frac{1}{4}$  or  $\frac{3}{8}$  of an inch. Place over the Petri dish a stencil of any design. The stencil may be made of cardboard. In the dark-room, an unexposed photographic plate is placed over the stencil and the entire preparation placed in a light-tight box. After twenty-four hours, the plate may be developed. A definite silhouette of the stencil will appear upon the photographic plate. (Fig. 2.)

The minimum time of exposure has not been ascertained, but after a few hours a definite impression is already visible.

The identical experiment repeated with petrolatum that has not been irradiated will not impress the photographic plate. It is evident, therefore,



FIG. 4.—Photographic impression from petrolatum irradiated through Uviol filter.

FIG. 5.—Impression from petrolatum, irradiated through Uviol filter and photographed through X-ray film hermetically sealed.

that irradiation endows petrolatum with certain properties which it did not have before and naturally, opened up a number of channels calling for further investigation.

In the first place, it could not be definitely asserted from the foregoing, that these newly endowed properties were supplied by the ultraviolet field of the spectrum.

In order to test this part of the problem, I took four Petri dishes, properly shielded from reflected and transmitted light and placed in each an equal quantity of plain petrolatum. Over one was placed a red-glass filter; over the second, a yellow-glass filter; over the third, a blue-glass filter; and over the fourth, an ultraviolet light filter, and exposed them all for one hour to the ultraviolet light.

At the termination of the exposure, I removed the filters and placed each dish in a separate, light-tight box. Over the dish containing the petrolatum exposed through the red-glass filter, I placed a cardboard stencil marked R,



and similarly over the dish containing the petrolatum exposed through the yellow, a stencil marked Y, and over the blue, a stencil marked B.

Over the petrolatum, irradiated through the ultraviolet filter, I placed a stencil marked U. V. F. Over each stencil, I placed a photographic plate. The boxes were closed and kept in a dark-room for twenty-four hours. At the expiration of that time, the four plates were developed.

The plate over the petrolatum that had been irradiated through the red-glass filter was entirely negative. The plate over the petrolatum that had been irradiated through the yellow-glass filter was likewise negative. The plate over the petrolatum that had been irradiated through the blue-glass filter was slightly positive. (Fig. 3.) The plate over the petrolatum that had been irradiated through the ultraviolet filter was intensely positive. (Fig. 4.)

This result is entirely as might have been anticipated. The red-glass filter permitted only red light to impinge upon the petrolatum to the exclusion of all other light. The yellow-glass filter permitted only yellow light to impinge upon the petrolatum. Radiations of the ultraviolet zone do not extend into the field of visible light.

Theoretically, the petrolatum irradiated through a blue-glass filter should also have been photometrically negative, if the newly imparted photometric property was due solely to the radiations from the ultraviolet zone.

The fact that petrolatum does become photometrically activated through a blue-glass filter proves that this endowment is contributed not only by the ultraviolet zone but also by a small range of the lower end of the visible spectrum.

The line of demarcation between the violet and the ultraviolet radiations is not a frontier, either from a theoretical or technical point of view, as there is no difference in the nature of the two types of rays. The line of demarcation depends upon the individual sensitivity of the retina.

The visible spectrum at its lowest point of visibility is established at 4,000 Angstrom units. The violet ranging into the deeper shades of blue reaches up to 4,500 Angstrom units, which is probably the upper limits of the visible spectrum which yield radiations that activate, photometrically, the mineral oils.

The lower limits of the ultraviolet zone which contribute this property to the mineral oils, are as yet undetermined but the Uviol filter, which was used in these experiments, permits the penetration of ultraviolet radiations to as low as 2,530 Angstrom units.

Petrolatum irradiated through an ultraviolet filter that eliminated all parts of the visible spectrum was tested out photometrically and was found to produce a very dense image.

It may be accepted, therefore, that the photometric property acquired by petrolatum by exposure to the carbon arc or to the mercury vapor arc is produced by radiations from the ultraviolet zone and to a small degree by radiations from the lower range of the visible spectrum.

Now, even though it is conceded, as I believe it may be, that ultraviolet

irradiation of petrolatum induces certain changes in that basic substance which effect a photographic plate, it does not necessarily follow that these secondary emanations fall within the zone of ultraviolet light nor in fact that the emanations are truly actinic in nature. We are accustomed to think in terms of physical chemistry but when we employ the agency of the ultraviolet light, we must transfer our thoughts to what is known of the science of electron physics.

Ultraviolet light is one of the most potent means of atomic dissociation or ionization and this is without doubt what occurs when petrolatum or other substances are irradiated. Atomic dissociation is the forcible tearing asunder of the atomic structure of the molecule, by striking off electrons from their molecular orbit and giving to the altered molecule a new speed of molecular vibration. It is quite conceivable, therefore, on the basis of electron physics that any susceptible material can be rendered radio-active and this seems to be the case. However, as many of the properties of these secondary emanations resemble those of light, it is difficult to prove that these emanations are really light waves, because in many respects they differ from the familiar properties that we are inclined to associate with luminosity.

In 1898, W. J. Russell<sup>2</sup> discovered that a large number of substances of most diverse character rendered a photographic plate developable. This phenomenon has since been referred to as the "Russell effect," "photechic effect," "Moser rays," "metallic radiations," etc. More recently, studies have been made by Kugelmass and McQuarrie,<sup>3</sup> West and Bishop<sup>4</sup> and others.

It is important not to confuse the so-called "Russell effect" with the discussion of the phenomenon described in this presentation. The "Russell effect" is a phenomenon of pseudo-actinism possessed by many materials in their natural state and is not the result of pre-exposure directly to the action of the ultraviolet light.

Kugelmass and McQuarrie have made careful studies of phenomena described as the "Russell effect" and believe that "the phenomenon is too difficult to isolate at present" but lean to the conclusion that "the active agency in this phenomenon appears to be a material substance rather than a radiation."

There are many reasons to believe that the reaction upon the photographic plate is caused by vaporous reducing agents of an oxidizing nature and I believe that in many of the instances reported such is the case. The phenomenon of which I speak is not a "Russell effect," for the reason that the photographic plate is acted upon through a hermetically sealed screen which eliminates effectively all oxidizing vapors, and can be ascribed to nothing else but to the transmission of electromagnetic radiations.

I have accomplished this by employing X-ray film from which the emulsion was removed, and sealing hermetically upon it, the photographic plate, by pouring paraffin about the edges of the plate. The X-ray film was cut in such manner that its edges extended far beyond those of the photo-

graphic plate. The photographic plate in that manner was securely shielded from any vaporous oxidizing substances and could be affected only by an energy that could pass through the X-ray film.

This preparation was then placed over a dish of warmed irradiated petrolatum with a stencil interposed and the entire preparation placed in a light-tight box and left for twelve hours. (Figs. 6 and 7.)

At the end of this time, the photographic plate was separated from the X-ray film by cutting through the paraffin binder and developed. A dense image of the stenciled lettering on the interposed cardboard appeared in great intensity.

The X-ray film is absolutely impervious to material emanation or any vaporous oxidizing substances; the paraffin binding is also impervious. There is not the slightest fogging of the unexposed portions of the plate.

This proof that irradiated petrolatum emits emanations that will penetrate a transparent material of the density of X-ray film, together with the fact that irradiated petrolatum will cause



FIG. 6.—Photographic impression from irradiated petrolatum through washed X-ray film, hermetically sealed.

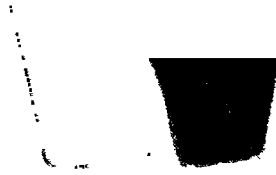


FIG. 7.—Photographic impression from irradiated petrolatum through X-ray film filter, after five days' exposure.

a wide divergent shadow to be caused by an object lying upon a photographic film, led me to the conclusion that the emanations emitted from irradiated petrolatum are truly electromagnetic in nature.

I believe also that there is a second factor which is of the nature of an organic emanation and the question of to how much of the one or the other is due the therapeutic value, must at present remain unanswered.

This secondary emanation, be it light waves or chemical, does not pass through a quartz filter. It will be argued, for that reason, that the emanations cannot be light waves because ultraviolet rays do pass through a quartz filter. This objection, however, is not valid because if these waves are light waves, they are of a secondary nature and need not necessarily have the same properties as primary ultraviolet rays.

In conclusion, referring once more to the therapeutic value of irradiated petrolatum, I wish to state that I believe its therapeutic virtue to reside

in a secondary radiant energy, endowed by its exposure to the ultraviolet light.

I have spoken only of its application in suppurative conditions and have stressed its bactericidal value. I have made no mention of a wide variety of uses in which I have found it of great benefit. Its possibilities are far reaching and time only will determine its limitations.

This preliminary report will in due time be followed by a more exhaustive description of clinical, physical and bacteriological studies together with a detailed description of the method of irradiation.

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# TRANSACTIONS

OF THE

## PHILADELPHIA ACADEMY OF SURGERY

STATED MEETING HELD FEBRUARY 2, 1931

The President, Dr. George P. Muller, in the Chair

Calvin M. Smyth, Jr., M.D., Recorder

### LOBECTOMY FOR BRONCHIECTASIS

DR. JOHN B. FLICK presented a man from whom he had removed the lower lobe of the right lung on account of its involvement in bronchiectasis and the consequent pulmonary hæmorrhages. The patient, a white male, aged thirty, was admitted to the Jefferson Hospital in July, 1927, because of pulmonary hæmorrhages. A previous diagnosis of tuberculosis had been made, but study showed a non-tuberculous bronchiectasis limited to the right lower lobe. (Fig. 1.) There was a history of a middle-ear infection at the age of two and a half years resulting in a chronic otitis media for which a mastoid operation was performed in 1912. He had pneumonia at eight years of age. In 1925, the tonsils were removed. The patient had had a chronic cough as far back as he could remember, but no previous attacks of blood-spitting. He was slightly improved by a phrenic exeresis performed in April, 1928, and by regular bronchoscopic drainage, but cough with offensive sputum and frequent attacks of hæmoptysis continued.

The induction of an artificial pneumothorax was attempted, but failed because of pleural adhesions. The patient was incapacitated for work and anxious to have something further done to alleviate his condition. A lobectomy in three stages was decided upon, the first two stages comprising a partial thoracoplasty and the third stage, excision of the involved lobe. The operations were done under nitrous-oxide anæsthesia. May 17, 1929, a subperiosteal resection of the posterior part of the eleventh, tenth, ninth and eighth ribs was performed through the incision ordinarily used in doing the lower stage of a paravertebral thoracoplasty. On May 29, a subperiosteal resection of the posterior part of the seventh, sixth and fifth ribs was done through an incision begun over the erector spinæ mass at about the level of the sixth rib and extended downwards and forwards over the seventh rib to about the mid-axillary line.

June 5 this wound was reopened and the bed of the seventh rib incised. The adherent lower lobe was freed chiefly by blunt dissection with the finger, but in one or two places the endotherm knife was used to divide adhesions. Where the adhesions were dense, their separation gave rise to a troublesome ooze which, however, was promptly controlled by hot packs wrung out of normal saline. The pulmonary ligament was divided and the lower lobe remained attached only by a narrow pedicle made up of bronchus, the vessels and some enlarged lymph-nodes. Two Number 3, forty-day, chromic gut ligatures were tied around the pedicle as tightly as possible and the lower lobe cut away, leaving only a short stump to hold the ligatures, which were left long. A small hole was made in a piece of rubber dam a foot square and the stump of the amputated lobe drawn through this opening and gauze

## LOBECTOMY FOR BRONCHIECTASIS

packed loosely around it within the dam. The edges of the rubber dam were brought out so that a funnel was formed around which the external wound was partially closed with three silkworm-gut sutures. Since the upper and middle lobes were adherent, there was no marked embarrassment of respiration. The pulse rate, however, rose to 160. For a few days after operation there was profuse serous drainage. This soon diminished and the drainage became purulent. The gauze packing was gradually removed and the rubber dam taken out June 22. July 1 the ligatures and a bit of necrotic tissue came away. The wound healed, leaving a bronchial fistula. December 27,

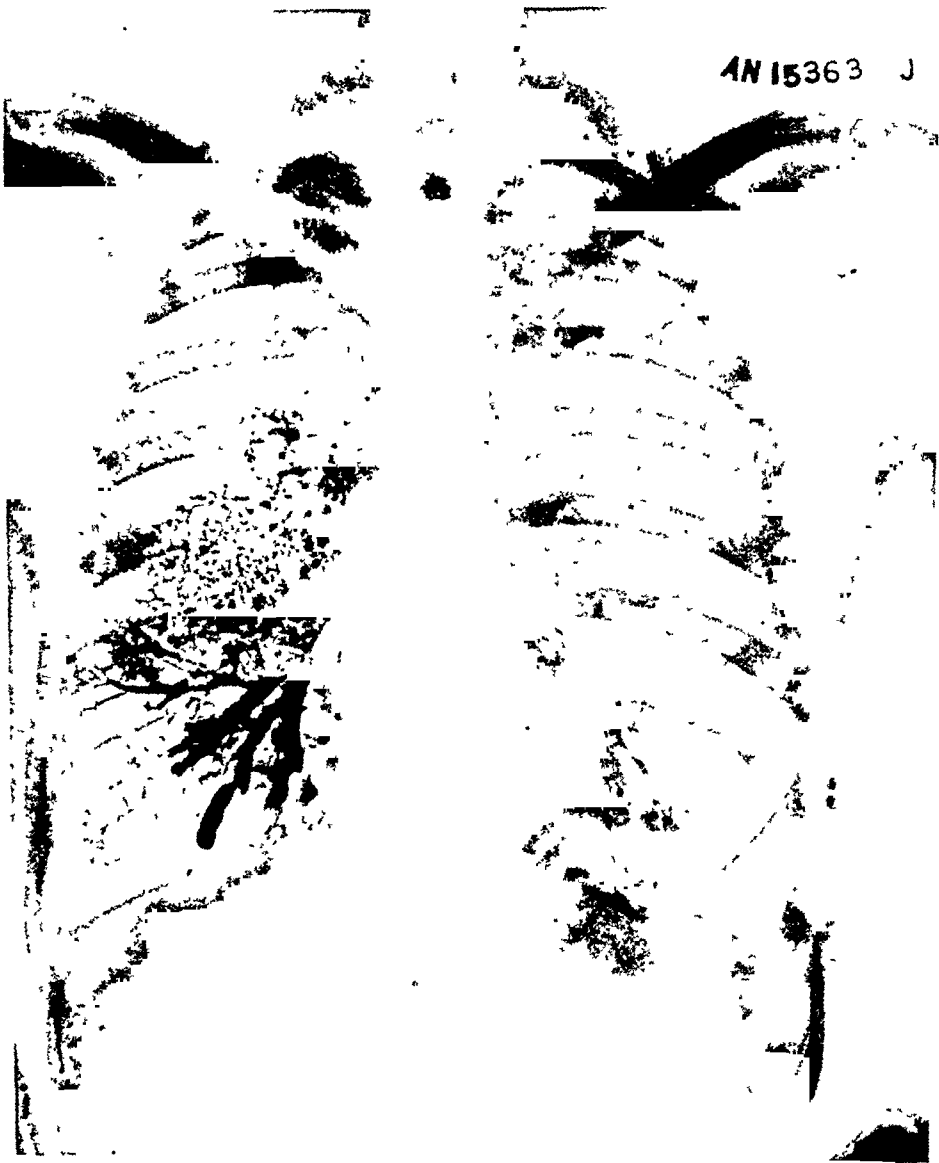


FIG. 1.—Röntgenogram after bronchoscopic aspiration and the injection of iodized oil showing the cylindrical bronchiectasis of the right lower lobe. (L. H. Clerf, W. F. Manges and J. T. Farrell, Jr.)

1929, the fistula having persisted, the regenerated seventh and part of the eighth ribs were excised, the fistula closed and covered with muscle. There was no recurrence of the fistula and the wound healed well. The patient has gained in weight, has had no hæmoptysis since operation and has very little expectoration.

A bronchoscopic examination made by Dr. L. H. Clerf January 22, 1931, showed no abnormal secretion in the right bronchus; the anterior extremity of the carina was slightly deviated to the right side; the orifice of the right upper lobe bronchus appeared more prominent than usual; the middle

bronchial orifice was practically normal in appearance. The lower lobe bronchus terminated in a pouch 2 centimetres beyond the orifice of the middle lobe bronchus; the bottom of the pouch presented two small, pitted depressions separated by a horizontal ridge.

#### NICOLA OPERATION FOR RECURRENT DISLOCATION OF THE SHOULDER

DR. DEFOREST P. WILLARD, presented a youth, aged nineteen years, who dislocated his left shoulder in November, 1928. Dislocation was anterior and was immediately reduced and kept at rest for four weeks. During the following winter and summer, under minor strain, the shoulder dislocated completely three times, and the patient had felt the bone slip anteriorly on numerous occasions. He stated that his arm was getting very much weaker, and that the shoulder-joint felt loose and was quite painful at times. The last dislocation occurred when the patient was rolling over in bed during the night. Examination in 1929, one year after first dislocation, showed slight atrophy of the muscles around the shoulder-joint. The head of the humerus could be moved forward easily, and also retracted away from the glenoid cavity about one-half inch. There was no limitation of motion and no swelling of the arm. January 16, 1930, the shoulder again dislocated, and on January 31, 1930, operation was done, following the method devised by Doctor Nicola, of New York, and published by him in the *Journal of Bone and Joint Surgery* for January, 1929.

The incision begins over the coracoid process and passes down over the anterior portion of the deltoid for four inches. The upper fibres of the deltoid are divided. The tendon of the long head of the biceps is exposed up to its origin. To do this it is necessary to divide the transverse humeral ligament. The tendon of the long head of the biceps is divided about one inch below the cut margin of the ligament. A hole is drilled through the head of the humerus, beginning just below the ligament, and is so directed that it emerges just above the centre of the articular surface of the head. The proximal portion of the tendon is then drawn through this hole and resutured to the distal end of the tendon and ligaments and soft parts closed. In this case the arm was bandaged to the side for three weeks, and then massage and active exercise started. In three months the patient was able to use his arm for golf. By July he had a full motion, which included use in swimming. During the Fall he has again played football without re-dislocation.

Two other similar cases during the year have given equally good results. The speaker believes that this operation has the simplest technic and gives the most permanent results of any operation so far used for this condition. The muscle function of the biceps is not interfered with, and, if the drill holes are accurately placed, the shoulder motion is not limited, except, perhaps, in extreme external rotation.

DR. T. TURNER THOMAS remarked that the original operation of choice was the excision of the head of the humerus—that did not last long, then came the contraction of the capsule, and that held sway for a great many years until comparatively recently when these suspension operations were introduced. The object is to make the operation simpler and safer than that for contraction of the capsule in which the surgeon must get down to the capsule, which is not easy in the anterior or subcoracoid dislocation.

## ANGIO-ENDOTHELIOMA OF THE HUMERUS

The approach must be in front, between the deltoid and pectoralis major muscles, or through the axilla. Clairmont, in the past, used a deltoid flap around the humerus to act as a sling, and later came gradually these suspension operations which are done on the outer side of the joint. The whole thing will hinge on the results. In the discussion of Henderson's paper, two of those discussing said that they had trouble with recurrences following the suspension. One (Carrell) added in the second operation after two such failures, contraction of the capsule by reefing with 100 per cent. success. One is still in the stage of wanting to know how much the shoulder will stand after these suspension operations.

DR. CHARLES F. NASSAU said that, while many surgeons have had the opportunity of operating upon recurrent dislocations, he did not feel that the various methods were certain enough to warrant operation. As soon as the speaker read the description of Nicola's operation, he determined to use it. Of all procedures devised it is the most mechanically perfect and the simplest. One great advantage of this operation is that it is not necessary to cut tendons or perform other mutilations.

DR. LOUIS D. ENGLERTH presented two X-ray plates to show the result four months after operation upon a woman of fifty-three years who obtained a perfect functional result following the Nicola operation.

## ANGIO-ENDOTHELIOMA OF THE HUMERUS

DR. ELDRIGE L. ELIASON reported the case of a man, aged thirty-two, who was admitted to the University Hospital March 31, 1930, with the history that fifteen months prior to admission he began to suffer pain in the right shoulder. Three months prior to admission he fell, striking right arm, which increased the amount of pain. Two months prior to admission a sudden pull on the arm resulted in an obvious pathologic fracture. Examination showed a fusiform enlargement of the right humerus at the junction of the upper and middle thirds. The enlargement was slightly less firm than the surrounding bone and there was preternatural mobility of the humerus at this point. Other extremities and bones negative. Gross physical examination, negative. After röntgenologic examination covering the entire osseous system, the growth of the right humerus was diagnosed as a probable sarcoma of the right humerus, with giant cells. Small periosteal elevation on the right ulna was diagnosed as fibrosing osteitis. Remainder of the osseous system and the chest were entirely negative for any further evidence of new growth or metastases.

April 2, 1930, two days after admission, the tumor growth of the right humerus was excised, and a portion of the left fibula selected and used as an intra-medullary bone graft, restoring the original length of the humerus.

The bone tumor itself was surrounded by an extremely thin shell of bone, and filled with thick granulations which bled profusely. These granulations were scraped out, and after squaring off the ends of the bone where they had been hollowed out in a cone-shaped manner by the tumor, the graft was then placed in position, and the thin shell sutured around it. The arm was dressed in plaster on a Mitteldorf triangle and internal right-angled splint.





Fig 1.—January 25, 1930 One day after the pathologic fracture

Fig 2—April 1, 1930. Approximately two months after fracture, and day prior to operation

Fig 3—November 10, 1930 Approximately seven months after operation

## TRAUMATIC EMPHYSEMATOUS BULBA

Fourteen days after the primary operation, the right ulna was exposed at the site of the small area of cystic change, and after chipping off the periosteum, a moth-eaten area of very hæmorrhagic nature was exposed. This tissue was similar to that found in the humerus. The bone was chiseled away down to healthy bone.

*Pathologic diagnosis.*—Angio-endothelioma of the humerus. Angioma of the ulna.

*Progress.*—Patient discharged April 22, 1930, twenty days after the primary operation. Four months later there was definite bony union and complete return of function.

## TRAUMATIC EMPHYSEMATOUS BULLA

DR. ELDRIDGE L. ELIASON reported the case of a man, aged forty years, who was admitted to the University Hospital August 2, 1930. Within a half hour prior to admission he had fallen ninety feet from steel-construction work, striking a workman standing on the ground below, the workman's head striking the patient in the epigastrium. Incidentally, the man standing below suffered a fracture of the spine to which he later succumbed. The patient was able to sit up at once, did not lose consciousness, and when admitted to the hospital complained only of sharp pain in the upper abdomen. The pain was entirely similar to attacks of acute indigestion suffered prior to the accident, and was somewhat paroxysmal. There was, in addition, slight pain in the left ankle and knee. The abdomen was flat, with considerable rigidity in the right upper quadrant and mid-epigastrium. Tenderness was marked over the same area. Peristalsis was entirely absent. Except for minor abrasions, the remainder of the physical examination was negative.

*Course.*—The patient continued to improve, but, on August 7, five days after the accident, he complained of a rather severe epigastric pain, rather continued and sharp in character. He was then examined under the fluoro-scope and X-ray films made. (Plate I.—August 8, 1930. Six days after accident.)

*Röntgenologist's opinion.*—"A collection of air above the right dome of the diaphragm, the identity of which is uncertain, but suggests a probable pneumothorax. A portion of one of the lobes of the right lung is collapsed. The identity of this lesion is uncertain; in some respects it looks like a localized pneumothorax, although all features are not explainable by this diagnosis. If this air is a localized pneumothorax, why does it not extend to the periphery? There is an area of increased density posteriorly which may be collapsed lung, but this also is not absolutely certain. If this patient has a large emphysematous bleb in the interlobar region, between the middle and lower lobes, it would partially explain some of the appearances. A localized pneumothorax with a previous adhesion of the lung would hardly explain it. There is no evidence of a diaphragmatic hernia of the stomach. We cannot exclude colon or small intestines."

The next day, fluoroscopic studies with barium could not demonstrate any evidence of intestines above the dome of the diaphragm. Good movement of the domes of the diaphragm was noted.

The patient was allowed to go home August 12, 1930, ten days after the accident. He was much improved, his abdomen soft and presenting normal peristalsis. Despite this, he felt rather "unstrung."

He was readmitted August 25, 1930, twenty-three days after the accident, because of nervousness and weakness. At that time expansion was limited on the right side of the chest. Breath sounds altered and diminished on the right, especially over the right lower lobe. Tactile and vocal fremitus noted

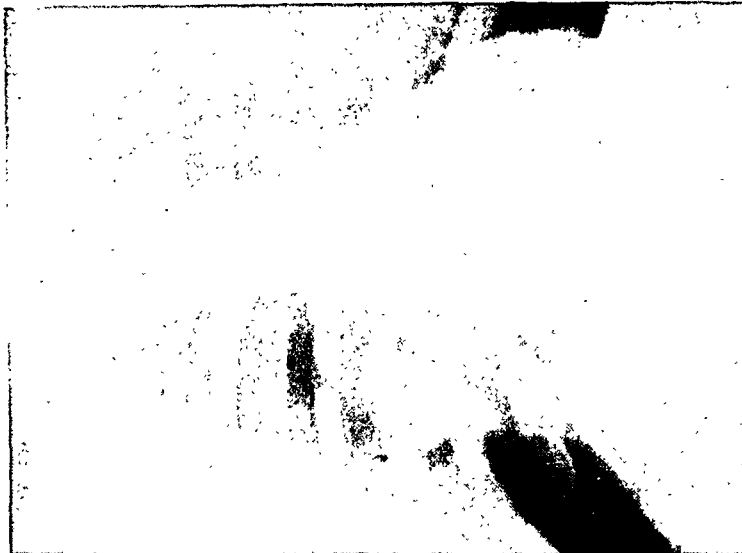


PLATE 3.—September 10, 1930. Approximately six weeks after accident. Approximately two weeks after last examination.



PLATE 2.—August 28, 1930. Twenty-six days after accident. Twenty days after last examination.

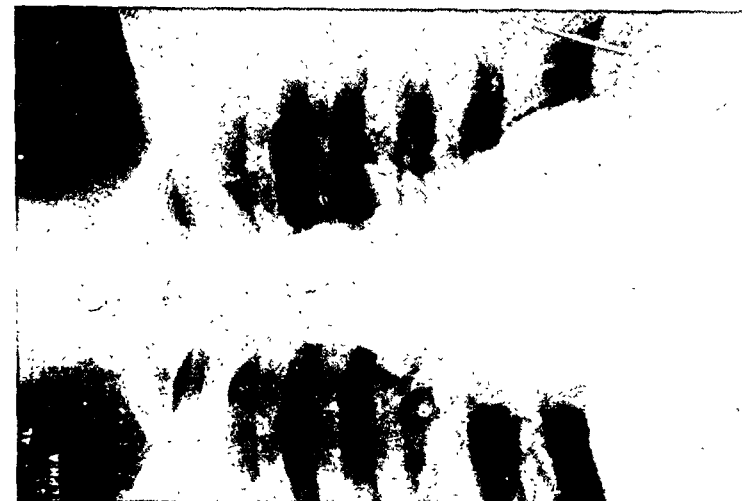


PLATE 1.—August 8, 1930. Six days after accident.

## TRAUMATIC EMPHYSEMATOUS BULBA

as being normal. Abdomen was negative. Remainder of physical examination was negative. Laboratory findings were negative. Chest X-rays taken. (Plate 2.—August 28, 1930.)

*Röntgenologist's opinion.*—"Pneumothorax, with complete collapse of the right lung. Large emphysematous bleb at right lower lobe. Examination shows complete collapse of the right lung with pneumothorax on this side. Just above the diaphragm there is a large cyst-like structure in the bottom of which there is a small amount of fluid. This is probably a large emphysematous bleb. The heart and trachea are somewhat displaced to the left side, causing some compression of the left lung. On inspiration, the heart moves to the right. There is paradoxical movement of the right dome of the diaphragm." The patient felt so much improved that he was permitted to go to his home on the date of the above examination. He returned again September 10, 1930, for chest X-rays. (Plate 3.—September 10, 1930.)



PLATE 4.—September 23, 1930. Approximately two months after accident. Approximately two weeks after last examination.

*Röntgenologist's opinion.*—"There has been some inflation of the right lung. In addition, the heart and the mediastinum have returned slightly to their normal position. The large emphysematous bleb is still approximately the same size. There does not appear to be any fluid at this time. There is, however, a slight pleural effusion at the right base." Patient was again readmitted to the hospital September 22, 1930, about two months after the accident, because of continued weakness, cough, and slight, occasional, bloody expectoration. The following X-ray studies were made. Plate 4.—September 23, 1930.)

*Röntgenologist's opinion.*—"Comparison of these films with those made on September 10, 1930, Plate 3, shows that the large annular shadow, previously mentioned in the lower third, has now extended to the upper half of the chest. It no longer contains any fluid. The lung in the lower half of the chest has reexpanded until it now occupies a position approximately 25 per cent. of the total pneumothorax volume in size, beneath the annular shadow described above. There is still a small amount of fluid at the base.

Left side shows no change. Heart and mediastinal shadow now occupy a more normal position." The patient was again permitted to go to his home September 24, 1930, much improved. He returned for two subsequent X-ray examinations. (Plate 5.—November 17, 1930.)

*Röntgenologist's opinion.*—"The patient still has a pneumothorax with complete collapse of the right upper lobe. The lower portion of the lung seems to be fairly well expanded. The right diaphragm is elevated and adherent, and possibly adherent to the pericardium. The emphysematous bulla is probably still present. The expanded lung seems to be quite dense, probably due to the retained secretions." (Plate 6.—December 8, 1930.)

*Röntgenologist's opinion.*—"The appearance is much the same as at last examination. The top of the bulla has reached the apex of the chest and probably can go no further. The lower portion of the right chest shows considerable thickened pleura, no doubt from the presence of air for so

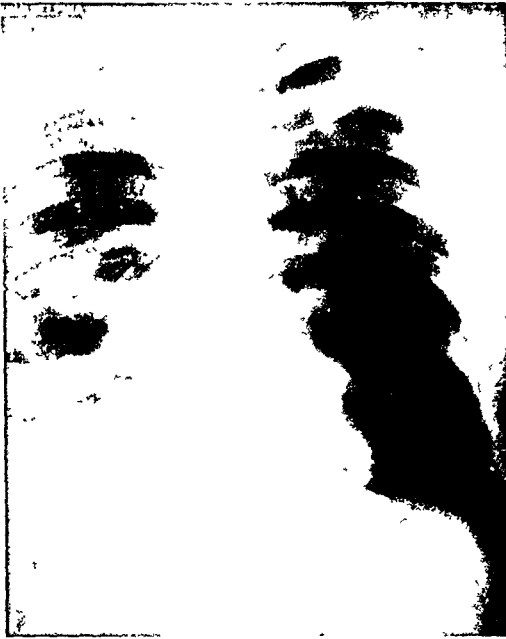


PLATE 5.—November 17, 1930. Approximately three and a half months after accident. Approximately two months after last examination.

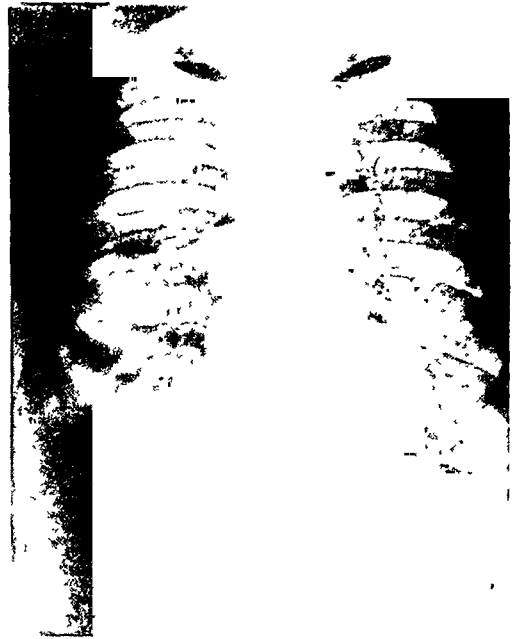


PLATE 6.—December 8, 1930. Approximately four months after accident. Approximately four weeks after last examination.

long a time, and also the presence of blood. With the patient lying on the right side, there is evidence of some fluid in the pleural cavity." The patient was then readmitted to the hospital, and an attempt made to pass a needle into the emphysematous bleb seeking to collapse it by evacuation of the air contents. This failed entirely. The patient was permitted to go home on the same day. The patient has not returned to his former occupation as a structural steel worker because of a nervous mental state, closely resembling what is commonly known as shell-shock. There was at no time no definite physical evidence of a fractured rib. The röntgenograms failed to conclusively disclose such. When the patient returned September 10, 1930, the following explanation of the bleb and its changes was offered. This röntgenologic opinion considered collectively the first four examinations.

"In reviewing this case, it is now evident that the first films taken on August 8, 1930, Plate 1, show a partial pneumothorax, consisting of the upper and possibly the middle lobes on the right side. Attached to the upper or

the middle portion of the collapsed lung there is a large pleural bleb which has been caused by the subpleural rupture of the lung. This bleb occupies a basal position because of collapse of the lobe to which it is attached. The lower lobe has not yet collapsed. In the films taken on September 28, 1930, Plate 2, there is complete collapse of all the lobes on the right, the bleb occupying its previously described position. Examination made on September 10, 1930, Plate 3, shows beginning expansion of the right lung, which has moved the bleb along with the lung tissue to a slightly higher position. In examination of today, September 23, 1930, Plate 4, this process has advanced to its position described."

Instead of this being a traumatic bleb, as we have intimated, could this defect be congenital, or possibly a large "ring shadow," some of which have been described?

DOCTOR ELIASON said that Doctor Pancoast reports that he had seen one other such case, discovered accidentally and not associated with trauma. In one work on surgery of the lungs, the speaker found a picture very much like this and it was used to describe the term employed in the book, "annular shadow," or pleural ring, and it was supposed to be an intrapneumonic pneumothorax or a dilatation within the lung proper filled with air. It has always been a question with Doctor Eliason whether the patient did not have this condition long before he fell the ninety feet.

DR. JOHN B. FLICK recalled a patient at the Jefferson Hospital who gave a history of a pneumothorax on the left side which followed a severe accident a year and a half prior. The pneumothorax developed, the patient said, about four days after injury and then gradually disappeared. He came to the Jefferson Hospital because of dyspnoea. Bronchoscopy showed a displacement of the tracheo-bronchial tree to the left and an atresia of the left bronchus. X-ray examination showed a massive collapse on that side. The speaker's conception of this lesion was that he probably sustained an injury to the hilum of the lung and that the resulting scar tissue completely occluded the left primary bronchus.

## INTRAVENOUS UROGRAPHY

DR. ALEXANDER RANDALL read a paper with the above title for which see page 1202.

DR. KARL KORNBLUM, by invitation, discussed the essential factors in the radiographic technic employed in intravenous urography. A representative series of röntgenograms illustrating the various urologic conditions in which this procedure is of diagnostic value was shown. This series included normal urograms, hydronephrosis, various forms of urinary-tract obstruction, anomalies, neoplastic diseases and the urinary tract in children. Methods of interpretation were discussed. It was emphasized that intravenous urography depicts the functional activity of the urinary tract. The method is not a short-cut to urologic diagnosis but is merely an adjunct to the well-established methods of diagnosis employed in urology.

## PHILADELPHIA ACADEMY OF SURGERY

DR. W. HERSEY THOMAS asked Doctor Randall if he had observed the specific gravities of the urines for the six hours following the injection. When uroselectan was first introduced, it was stated that if the specific gravity of the urine did not rise above 1038 during the second and third hours following the injection, the renal function was below normal. This was not corroborated by Doctor Thomas's experience. In some cases with good renal function the specific gravity of the urine did not reach 1038. In other cases, with admittedly poor renal function, the uroselectan was secreted so rapidly that most of it reached the bladder within fifteen minutes. With the latter group of cases in mind it is therefore Doctor Thomas's practice to make the X-ray exposure five minutes after the injection, instead of fifteen minutes as recommended by Doctor Randall, and he feels that by following this modification of the technic, information is often obtained that would otherwise be missed.

### SURGICAL TREATMENT OF BLEPHAROSPASM

DR. CHARLES H. FRAZIER read a paper with the above title for which see page 1121.

DOCTOR FRAZIER, replying to questions, discussed the anæsthesia problems pertaining to the subject. In some cases, the preliminary dissection was made under nitrous oxide. In two cases, however, he used local anæsthesia (novocaine) and in doing so he thinks made a mistake. The novocaine, he felt, desensitized the nerves so that they did not respond to electric stimulation. Thus, at once a means of identification, upon which he must rely in the selection of branches to be cut, was removed. He therefore recommended the nitrous-oxide anæsthesia for the preliminary dissection to be discontinued as soon as the various branches have been exposed. It is desirable to continue the operation with the patient conscious, so as to determine when sufficient nerves have been cut to paralyze the orbicularis palpebrarum. This can be determined only by instructing the patient to close or try to close the eye. The speaker added that in four out of six operations the patients could close their eyes, although only feebly. This residual movement he has not been able to explain since he was quite sure no nerve filaments were left uncut along the superior or upper anterior margin of the parotid gland itself. Of course, the buccal division itself must be left intact, as, if cut, the angle of the mouth would sag. But one must remember that, in some cases, the buccal division gives off one or more branches which supply the orbicularis palpebrarum. No patient has developed trophic ulcer.

# TRANSACTIONS

OF THE

## NEW YORK SURGICAL SOCIETY

STATED MEETING HELD JANUARY 14, 1931

The President, DR. EDWIN BEER, in the Chair

### PIROGOFF AMPUTATION OF THE FOOT; NINE YEARS POST-OPERATIVE

DR. JOHN C. A. GERSTER presented a man, fifty-eight years of age, who, in April, 1922 suffered partial traumatic avulsion of the foot. The tarsus and metatarsus were denuded of skin and subcutaneous tissue, and were covered with granulations. There was just enough normal skin around the ankle and heel to permit the performance of a typical Pirogoff amputation which was done on May 13, 1922. To prevent accidental soiling of the operative field a very thick pad of iodoform gauze was used to cover the suppurating granulating stump, so that the skin incision and subsequent stages of the Pirogoff amputation could be performed aseptically. The patient made an uneventful post-operative convalescence and has been well for the past eight and one-half years.

The case was presented because of its relative rarity.

DR. HENRY H. M. LYLE said that Pirogoff led an active surgical life and among his many contributions to surgery his osteoplastic amputation (1852) was not the least. Pirogoff's operation is the first recorded osteoplastic amputation. Contrary to what most writers have claimed Pirogoff attached only secondary importance to the osteoplastic feature; his main endeavor was to devise a procedure which would overcome the difficulties encountered in dissecting out the os calcis. Pirogoff's stump is superior to Syme's; it is longer, permits of an early functional use, has little or no tendency to atrophy, is not painful. As the origin and insertion of the gastrocnemius are both intact, the combined movements of the knee and ankle make running and other exercise possible. It is not difficult to fit with an artificial foot. The speaker had used an ordinary walking shoe with a sling strap and found it perfectly satisfactory. The objections advanced against this operation were that it is difficult to perform; it is unsuitable in diseased conditions; the os calcis may fail to unite and necrosis is apt to occur. The results of the last war have shown that where this operation has been indicated and performed with ordinary skill it yields a splendid functional and painless stump.

### POTT'S FRACTURE WITH PERSISTENT POSTERIOR DISLOCATION OF ASTRAGALUS; SIX YEARS AFTER REDUCTION

DR. JOHN C. A. GERSTER presented röntgenograms of a man aged sixty-two, who was admitted to the Lenox Hill Hospital, service of Dr. DeWitt



Stetten, February 18, 1924. He had sustained a Pott's fracture of the left ankle shortly before admission. There was a great deal of subcutaneous effusion and swelling, involving not only the ankle but most of the leg. X-ray showed a posterior lipping fracture of the lower end of the tibia. Several attempts at reduction and immobilization in plaster failed. Finally, February 23, five days after admission, it was decided to try suspension of the foot with a support under the knee, trusting the weight of the leg itself would maintain proper reduction. This was found to be effective and suspension was maintained for four and one-half weeks. During this entire time the patient obeyed instructions to flex and extend the ankle-joint. Suspension of the foot was accomplished by a slipper of adhesive plaster fitting the sole of the foot and the back of the heel, kept in place with a snug bandage.

March 27, four and one-half weeks later, he was allowed out of bed with no weight-bearing.

April 10, he bore weight on his foot and on April 16 was discharged, walking without pain.

The posterior lipping fractures of the tibia are difficult to reduce; the astragalus showing a tendency to slip backward on the lower end of the tibia. It would seem advisable to try this method of suspension of the foot before resorting to tenotomy of the tendo Achillis. This patient was presented some years ago and is again presented complaining of no disability and with no symptoms of late arthritis.

This case was presented before the New York Surgical Society April 23, 1924, *ANNALS OF SURGERY*, vol. lxxx, p. 634, October, 1924; also *ANNALS OF SURGERY*, vol. lxxxvii, p. 450, March, 1928.

DOCTOR GERSTER said he had occasionally found it convenient to use this method in reducing a Pott's fracture with slight displacement, suspending the foot in the manner described, using an orthopædic table. As the patient's muscles gradually tired it became possible to reduce the fracture and maintain reduction with molded plaster splints. All this without general anæsthesia. In one case, with very marked displacement, requiring general anæsthesia, the foot was suspended. Anæsthesia was then begun. The surgeon was called out of the room for the moment. On his return, the fracture had reduced itself, as relaxation under anæsthesia supervened, and the weight of the obese lower extremity became effective. Nothing remained except to apply plaster. A control X-ray, the following day, showed perfect apposition of fragments.

#### CARCINOMA OF RECTUM

DOCTOR GERSTER presented a woman, aged forty, who was admitted to the service of Dr. A. A. Berg, Mount Sinai Hospital, May 4, 1927, with a history of one year's progressively increasing constipation, much worse during the past six weeks. Three weeks ago, blood and mucus in stool for the first time. Had lost 25 pounds in past year. Present weight, 80 pounds.

Physical examination showed small emaciated woman, in fair general condition. Hæmoglobin, 70 per cent. Otherwise negative, except for a rectal mass, 1½ inches above sphincter.

At laparotomy May 25, 1927, a carcinoma of the rectum was found, adherent to the posterior wall of the uterus. Consequently a supravaginal hysterectomy was first made. The uterus loosened from the tumor in the

course of operative manipulations. The rectosigmoid was mobilized; the tumor-bearing gut was then packed in the pelvis, and the pelvic peritoneal diaphragm was then reestablished, accurately suturing the peritoneum to the wall of the sigmoid as it passed into the true pelvis. The abdominal wall was closed in layers. The patient was then turned on her side in Sim's position. A median incision with its centre over the coccyx was then made. The coccyx was removed and the pelvic cavity was entered. The tumor-bearing loop of gut was delivered posteriorly and the afferent and efferent loops were sutured parallel to each other. A series of black silk marking sutures with ends left long marked the level at which the subsequent amputation was done by Doctor Lewisohn in the absence from the city of Doctor Gerster. The spur was later divided with a crushing clamp and the patient allowed several months' convalescence before closure of the sacral colostomy.

The patient was presented at a meeting of the Surgical Section of the Academy of Medicine, January 6, 1928 (*Amer. Jour. Surg.*, N. S. iv, p. 444, 1928).

December 2, 1929, she was admitted to the Lenox Hill Hospital, service of Dr. DeWitt Stetten, complaining of difficulty in moving her bowels. Naturally, the possibility of local pelvic recurrence was considered, but digital pelvic examination under general anæsthesia on December 3 failed to reveal any typical masses.

A barium meal was given on December 5, which showed that the loops of sigmoid beneath the pelvic diaphragm in the true pelvis were fixed in dense adhesions and consequently had their normal peristaltic movement greatly hampered. This condition clearly accounted for her difficulty in having free evacuation of the large intestine.

This fixation of pelvic loops as well as the possibility of inadequate circulation after mobilization must be kept in mind when considering the advisability of performing a Mikulicz volagerung for a low rectosigmoidal carcinoma through a sacral opening.

DR. ALLEN O. WHIPPLE remarked that the measure of the level of a growth by digital examination may be a very deceptive thing. He had recently had an experience in which what was thought to be a low growth proved to be really in the sigmoid which had telescoped into the rectum. Doctor Whipple further inquired whether the growth, particularly if low down in the pelvis, would not offer considerable difficulty in the delivery through the sacral vent. Another point was the lapse of time between the application of the Mikulicz clamp and closure of the fistula. This sometimes takes a long time to close when the clamp is applied in the abdomen and Doctor Whipple wished to know what the duration was in the sacral region.

DOCTOR GERSTER agreed with Doctor Whipple that a growth which seems low to the examining finger may prove at operation to lie much higher than one would imagine from examination. A recent case of his illustrated this point. The tumor of the rectum could be felt just above the prostate, yet at laparotomy, the anterior surface of the tumor was in contact with the posterior wall of the bladder and below the lower margin of the growth there was an inch of normal rectal wall covered by peritoneum.

Regarding difficulty of delivering tumor-bearing gut through the sacral opening, in the particular case, just presented, the conditions were unusually

favorable. A small woman with a large pelvis and the growth itself not very large. Division of inferior mesenteric vessels to facilitate bringing of tumor-bearing loop lower is uncertain and risky. In this case, however, the vessels could clearly be seen to beat in the intestinal wall adjacent to the tumor after division of the main inferior mesenteric vessels between ligatures.

The sacral fistula was allowed to remain open for four months. At the end of this time, the opening had contracted to one-third its original size. The plastic closure was then very easy. She was kept constipated for a week afterward. There was no leakage.

#### PERFORATED GASTRIC ULCER

DOCTOR GERSTER presented a man, aged fifty-two, who was admitted to the Lenox Hill Hospital, service of Dr. DeWitt Stetten, July, 1922, on account of an acute perforation of a pre-pyloric gastric ulcer on the anterior surface  $\frac{1}{2}$  inch from the pylorus. It had perforated about eight-ten hours prior to admission. There had been a history of gastric distress for twenty years and eight years previously a large gastric hæmorrhage had occurred (1914). The perforation was closed with a single silk mattress suture and the patient made an uneventful convalescence.

A year later (August, 1923) he was again admitted with a history of renewed gastric complaints suggestive of retention. There was vomiting of food taken the previous day, and marked loss of weight. X-ray showed a greatly dilated stomach, with twenty-four-hour residue.

August 16, 1923, a Finney pyloroplasty was done 3 fingers wide. He made an uneventful convalescence and on the eighteenth day after operation stomach emptied in three and one-half hours. Two and a half years later (December, 1925) he experienced pain for about twelve hours similar to that he had suffered from just before perforating three and one-half years previously. At the time of examination six hours later, there was no subjective pain and no tenderness on palpation. However, six hours after this, there was massive gastric hæmorrhage. He remained in the hospital five weeks, made an uneventful convalescence, and X-ray taken just before discharge showed rapid emptying of the stomach. In the fall of the same year (1926) he began to have severe attacks of asthma, particularly at night; for which he was again admitted to the hospital and received treatment. In addition to his asthma, which continued for the next two years, massive gastric hæmorrhages would occur every few months. In June, 1927, he was admitted to the Lenox Hill Hospital for such a hæmorrhage. At this time, when convalescent, an X-ray showed slight six-hour retention in the stomach. During this period he also was admitted to the Coney Island Hospital, to the City Hospital at Welfare Island, and to the Long Island College Hospital, for recurrent massive gastric hæmorrhages. Gastric analyses in 1925 showed free hydrochloric acid 36, total acid 55. In 1927 free hydrochloric acid 50, total acid 60.

In February, 1928, he was again admitted with a history of epigastric pain, nausea, and vomiting of four and one-half months' duration. Gastric X-ray showed a large six-hour residue. February 11, 1928, under local anæsthesia a posterior suture gastroenterostomy was performed. At this time the site of the Finney pyloroplasty was found narrowed to the thickness of a ring finger. There was no sign of ulcer.

March 5, X-ray showed prompt emptying of the stomach through the stoma. Discharged March 19, 1928, after uneventful convalescence. Since

## TRANSDUODENAL CHOLEDOCHOTOMY; DUODENAL FISTULA

this time he has had no further hæmorrhage or gastric complaint. The asthma continued until October, 1928, when he received four bronchoscopic treatments one week apart. Since that time which is now over two years and a quarter, he has been well.

DOCTOR GERSTER called attention to the following points of interest in this case:

When the stomach was opened at the time the Finney pyloroplasty was being established, the silk mattress suture marked the point of previous perforation, and the mucous membrane opposite this point was freely movable, absolutely normal in appearance and showed no scarring although the perforation was one centimetre in diameter.

The various massive gastric hæmorrhages followed periods of long exhaustive manual labor over several months. He would sometimes work sixteen–eighteen hours a day.

For the past two years he has been fortunate in obtaining employment which did not require any physical exertion.

The recurrence of pyloric stenosis five years and a half after a pyloroplasty 3 fingers wide, seems unusual.

This patient was presented before the New York Surgical Society on October 10, 1923 (ANNALS OF SURGERY, vol. lxxix, p. 146, Case III, January, 1924) and also on March 24, 1926 (ANNALS OF SURGERY, vol. lxxxiii, p. 861).

STATED MEETING HELD JANUARY 28, 1931

DR. HENRY H. M. LYLE in the Chair

## TRANSDUODENAL CHOLEDOCHOTOMY; DUODENAL FISTULA

DR. FREDERIC W. BANCROFT presented a middle-aged woman who was admitted to the Fifth Avenue Hospital January 14, 1928, complaining of intense pain in the right upper quadrant. Three weeks before admission she had developed nausea and vomiting of yellow bile. Since that time she has had a continuous dull pain with occasional acute exacerbations and return of vomiting. Stools have not been noted as to color, but the odor is foul—with considerable gas. Pains occur in the right upper quadrant radiating to the right scapular region; are intermittent and occur three or four times daily. She has had occasional chills with sweats and fever during acute attacks. She was operated on two years ago for gall-bladder disease. She was in the hospital three weeks. The wound drained a greenish material for two months. Five weeks after the operation she had an acute attack which was just like the one prior to operation. When admitted she had exquisite tenderness in the epigastrium over the gall-bladder region. She had slight jaundice of the conjunctiva.

January 23, 1928, she was subjected to a transduodenal-choledocholithotomy with partial cholecystectomy and choledochostomy. There were dense adhesions of the stomach and duodenum and transverse colon to the liver, which were separated with considerable difficulty. At the gall-bladder fossa, a sac about 2 centimetres in diameter and 5 centimetres long with chronically thickened walls was found. A piece of the end of this, which apparently had a lumen, was excised and sent to the laboratory for diagnosis. Report returned was part of gall-bladder wall. Partial cholecystectomy was then performed. A stone impacted in the common duct near the papilla of Vater was removed through an incision in the duct.

At the conclusion of the operation yellow bile was escaping through

the tube into the common duct. Levin tube inserted through the nose to control post-operative vomiting.

*Post-operative Course.*—On the fifth post-operative day the patient had a chill, with a temperature of  $103^{\circ}$ , rapid respiration. She had been draining bile through her wound, but in the last twenty-four hours this had taken on a marked irritative character, so that the skin was reddened and there was evidence of some erosion of the muscle. Methylene blue was given by mouth, and appeared on the dressing within two hours.

On the following day the discharge from the wound was very profuse, clear in character, but did not contain any food particles.

On the 29th it was decided to follow the treatment suggested by Potter, which is as follows:

The wound was first dried with cotton and then washed with 1/10 normal hydrochloric acid. On top of this was packed gauze saturated in a heavy meat extract and olive oil. This procedure was repeated every two hours, with the idea of neutralizing the alkaline pancreatic juice and exhausting its digestive effect. In addition, as the patient was losing a great deal of fluid, she was given 3,000 to 4,000 cubic centimetres of saline per day by clysis.

Five days afterward the wound appeared clean, the skin was not irritated, and there was practically no discharge. Four days later there were only 2 ounces of drainage in twenty-four hours. At the end of a week the wound was completely healed, the patient was up and about, and ready to be discharged.

This case is shown because of a rare complication of duodenal leakage following a transduodenal-choledocholithotomy. The fistula closed rapidly by Potter's treatment of hydrochloric acid and beef juices with olive oil.

DR. JOHN A. MCCREERY emphasized the use of meat extract, hydrochloric acid and olive oil in these cases. He had seen these used in two cases of duodenal fistula and the comfort of the patient, the rapid healing and the general improvement following the use of this method was striking.

DR. THOMAS H. RUSSELL recommended the use of aluminum powder to be dusted around on the wound and spread with an applicator. This acts as a most efficient protective. This powder can be bought in any paint shop, is cheap and harmless.

#### GIANT-CELL SARCOMA LOWER END OF THE RADIUS

DR. FREDERIC W. BANCROFT presented a woman who was admitted to the New York Hospital in May, 1917. Two and a half months before she had fallen and sprained her wrist, but during the following week there was no pain. Then the wrist became tender on pressure. The tenderness gradually became worse. About three weeks ago she fell against the window of a car and dorsally flexed her wrist, which resulted in excruciating pain. The terrific pain continued.

Her surgical condition showed a swollen and reddened wrist which was very tender, especially over the prominences of the radius and ulna posteriorly. Scarcely any flexion in the wrist-joint and very slight flexion of the fingers; no crepitation and only a brawny induration over the head of the radius posteriorly. X-rays show marked rarefaction of the lower end of the radius.

June 4, 1917.—A longitudinal incision 7 centimetres long over dorsal surface of radius was made. Tendons retracted. In dissecting through ten-

## GIANT-CELL SARCOMA LOWER END OF THE RADIUS

dons considerable amount of clear, slough-appearing material escaped through a small hole in the radius. This hole was enlarged and a cavity was found in the head of the radius extending almost to the articular surface. This was smooth-walled and did not bleed. Another rupture had taken place on the anterior surface. Considerable amount of grayish material was curetted out. Cavity filled with Mosetig Morehof's bone wax. Tendons and fascia sutured over defect. Wound closed with continuous silk; no drainage. Anterior molded splint applied.

April 2, 1918.—Examination revealed the old scar over the dorsum of the right wrist, with diffuse swelling over the lower end of the radius. This was fusiform in shape, and bulging on all sides. There was no redness or fluctuation. There was tenderness over the end of the radius. There was limitation of wrist-joint motion in all directions, but no ankylosis. No limitation of motion of the fingers. No other bone deformities of the extremities detected.

April 3, 1918.—Through a posterior vertical incision the tendons were dissected free from the posterior surface of the radius, which exposed a reddish tumor mass projecting from the radius about 0.5 centimetre. This was excised and the cavity in the radius opened. It was filled with a mixture of bone paste and a reddish friable pulpy mass that appeared like giant-celled sarcoma. This was entirely curetted out. It was observed that there was a small perforation on the anterior surface of the radius. Cavity swabbed out with pure carbolic acid. Hæmostasis obtained. Three pieces of radium—one of 50 millimetres and two each of 25 millimetres then inserted into the cavity and closed over. The remainder of the cavity was filled with bone wax. Subcutaneous tissue closed with interrupted catgut; skin with silkworm gut and silk. Anterior molded splint applied. The radium was removed in five hours.

Subsequent history was that a small sinus occurred on the dorsum of the wrist. This discharged a small amount of purulent material mixed with bone wax. The patient was then treated by a radiologist, and developed an extensive X-ray burn so that her hand had to be kept in extension for several months. She was treated in another hospital and amputation advised, but she refused.

The X-rays showed no signs of recurrence of the growth. There was, however, marked limitation of the flexion of the fingers due to the atrophy from the long period of disuse when the hand was kept in a splint. As the X-ray showed a small osteomyelitic process in the lower end of the ulna, it was thought advisable to do a resection of the lower end of the radius and ulna, which was done on January 5, 1920. A resection of 2 inches of lower end of radius and ulna was performed.

May 2, 1921, a fourth operation (freeing of extensor tendons and plastic on dorsum of wrist) was done.

This case is presented because the primary tumor was of a type slightly more malignant than the usual giant-celled sarcoma in that the stroma about the giant-cells showed a more active process. While her result at the present time is not complete functional cure, it is very much more satisfactory than an artificial hand would be, and as thirteen years have elapsed, it seems reasonable to assume that there will not be a recurrence. The X-ray shows an anterior dislocation of the wrist, but she is able to drive a car, swim, and perform her ordinary duties and earn her living. The tumor at the original operation was yellow in type. The recurrence was, however, of the red, beefy, hæmorrhagic type. It has been suggested that the yellow type, which is more

closely related to the xanthoma type of sarcoma, is more malignant than the red type which has been described by Barrie as hæmorrhage osteomyelitis. Microscopically both sections showed numerous giant cells and an active stroma containing numerous spindle-shaped connective-tissue cells.

COFFEY OPERATION FOR TRANSPLANTATION OF URETERS:  
UROSELECTAN: PERINEPHRITIC ABSCESS

DR. FREDERIC W. BANCROFT presented a woman, aged forty-two, who was admitted to the Fifth Avenue Hospital November 28, 1928. Her history at that time was that she had had six operations for attempted repair of a vesicovaginal fistula. The last one was four years ago. She had had two pregnancies, the first one a stillbirth, at which time the fistula was created fourteen years ago. The patient is otherwise in satisfactory health.

The vaginal floor is a mass of contracted scar tissue, so that the vagina is very shallow and at the point where the urethra should open there is an opening about 2 centimetres in diameter which admits the finger into the bladder. The urethra and its sphincter are replaced by this fistulous tract with continuous urinary drainage. Doctor Furniss saw the patient in consultation. His note reads as follows: "Finger enters directly into bladder. Anteriorly there is only mucous membrane over the sub-pubic arch. Whole urethral sphincter gone, as well as posterior urethral wall. Do not believe any form of plastic repair will give a satisfactory result. Suggest Coffey implantation of ureter into rectum." Doctor Barringer also believed at this time that there was no possibility of creating a repair of the fistula. Transplantation of the ureters into the sigmoid (Coffey operation) was therefore determined upon. As a sigmoidoscope with a special light was to be used, the first part of the operation was carried out under ether and after completion of rectal part, patient was switched to ethylene.

Left para-median incision from pubis to about  $\frac{1}{2}$  inch above umbilicus. On opening the peritoneum the sigmoid was carefully inspected. It had some adhesions on the left side to the left of the pelvis. On freeing these it could be easily brought up into the wound. It had a very fat mesentery and there were numerous fatty epiploica at its right margin. Pelvis was contracted. Intestines were brought well out of the pelvis with the exception of the sigmoid and held back with pads. A soft rubber tube clamp was applied across the bowel at the colo-sigmoid junction. Patient was then drawn down to the edge of the table, sigmoidoscope inserted and pushed upward, directed by operator's hand in the abdomen, to within 1 inch of the clamp. The obturator of the sigmoidoscope was then withdrawn and a Lindeman needle attached to a syringe was inserted from abdominal side through sigmoid wall and sigmoidoscope withdrawn to within about 2 inches of the anal orifice. Irrigation with plain water first until returns were clear, then about 500 cubic centimetres of mercurochrome were inserted, allowing it to flow out through sigmoidoscope. Sigmoidoscope then reintroduced up to 1 inch of the clamp and gauze packing introduced, guided by the operator's hand, sigmoidoscope being withdrawn as gauze was inserted. Sigmoidoscope removed and patient then put in Trendelenburg position and both ureters were isolated at the bifurcation of the common iliac vessels and dissected downward beneath the broad ligaments to within about  $\frac{1}{2}$  inch of the bladder, then cut between Kocher clamps and distal ends cauterized and ligated. Proximal portion of the ureters with clamp attached then drawn up and laid along the sigmoid in a position without tension to show where the incision should be made. A longitudinal incision was then made in the

left ureter immediately proximal to the clamp and a No. 12 ureteral catheter carried upward about 6 inches. The ureter was tied around a rubber rider on the catheter with two linen sutures and again immediately proximal to the rider with one linen ligature. Left ureter was first anastomosed by making a  $1\frac{1}{2}$ -inch incision in the sigmoid down to the mucous membrane. At the distal portion of this incision a small nick was made in the mucous membrane, mosquito clamp introduced and piece of gauze in rectum drawn up. The end of the catheter was tied to this piece of gauze by the use of a linen suture on a curved needle which was passed through the gauze and the catheter. The assistant at the rectal end then gently withdrew gauze, the abdominal operator threading ureter's way through the orifice until the catheter and the ureter were introduced into the sigmoid beyond the rubber rider. It lay in this position apparently without tension. The sigmoid was united over the ureter with two interrupted No. 000 chromic sutures which also included a part of the ureteral wall. Remainder of incision in the sigmoid was closed with a No. 00 chromic stitch; a second continuous inverting suture was used. Peritoneum was united over the ureteral course as far up as it had been exposed, also the orifice of the peritoneum where the ureter had previously lain was closed with a similar stitch.

Similar procedure was adopted on the right side, incision being somewhat higher on the sigmoid and sigmoid had to be drawn slightly to the right side to relieve tension. Entire rectal gauze was removed after distal end of the catheter had been drawn outside the rectum. Peritoneum closed over ureter as on the left side. Abdominal wound then closed in layers in routine manner without drainage. Both catheters protruded outside the anal orifice about 6 inches and were separately united to rubber tubes so that the character and amount of drainage could be estimated.

The patient's immediate convalescence was uneventful: The catheters came away on the eighth day post-operative. She left the hospital seventeen days post-operative, with the wound completely healed and she getting up only twice at night.

*Follow-up.*—Patient did extremely well for about eight months, when she came back complaining of severe pain in the right lumbar region. She was admitted for study, with the idea of having uroselectan films taken. However, her blood urea at this time was up as high as 50, and for this reason it was postponed.

She was again readmitted August 6, 1930, with pain and distention of the right side of the abdomen. On admission her temperature was  $102.2^{\circ}$ . There was a large, painful mass in the region of the right kidney and it was thought that the patient probably had a pus kidney. An attempt to catheterize the kidney through the rectum was unsuccessful. Uroselectan was injected intravenously, and the following is her X-ray report of August 10, 1930:

"Films of the kidney tract after the injection of uroselectan show the following findings:

"The left kidney shadow is very small and somewhat obscured by gas in the intestines. There is a faint shadow which corresponds to the pelvis and calyces, but this is very faint. The shadow of the kidney is smaller than a normal sized kidney.

"There is a large mass in the right side of the abdomen which appears to spring from or is attached to the lower half of the right kidney. The pelvis and the upper and middle calyces of the right kidney are filled with solution and the upper calyx is definitely dilated; the pelvis shows a slight bulge suggesting dilatation. The lower calyx does not fill and the mass is



in this region which may account for the non-filling of this calyx. The mass is probably a cyst of the kidney or a tumor."

Two other uroselectan rays were taken, on the fifteenth and twenty-second respectively. Both corroborated the findings that the left kidney was very small and that a large tumor mass was apparently below the pelvis on the right side. For this reason it was considered that it was probably a perinephritic abscess. Therefore, on August 23, 1930, Doctor Carleton made a 6-inch incision in the right flank directly over the mass. More than a pint of pussy fluid was removed. He states that the condition was a perinephritic abscess located below and behind the kidney, pushing the kidney over toward the mid-line. Two large rubber tubes were inserted. The patient had a remarkably smooth post-operative convalescence following this, and was discharged on her sixteenth post-operative day with instructions to return to the Out-Patient Department for dressings.

She is now presented as a case of transplantation of both ureters two years ago, complicated later by a perinephritic abscess on the right side and a possible atrophy of the kidney on the left. The incision and drainage of the perinephritic abscess six months ago has resulted to date in a relatively healthy patient.

DR. HENRY DAWSON FURNISS (by invitation) said that this case illustrates the good results which can be secured with the Coffey operation in cases of extensive vesicovaginal fistulæ. The patient presented has evidently been made very comfortable by this procedure. In any case which evidently cannot be repaired with a satisfactory functional result, the patient should not be put through the great number of plastic repair operations so frequently done; but the procedure of Doctor Bancroft's should be followed. As to the primary mortality, this has fallen to a very small point. Unless there is some marked dilation of the ureter or infection, the chances of primary mortality should not be over 2 or 3 per cent. The point comes up as to what will happen to them eventually: the majority develop obstruction of the ureter and dilation. Pyelitis may occur, with dilation of the kidney pelvis. This brings up a point as to renal counterbalance. Hinman found that if he experimentally produced stricture of ureter the kidney very soon became functionally inactive. But, if he took out the other kidney, the injured one continued to function. In other words, a kidney will work if it is the only one. This is encouraging in those cases where it is necessary to remove a kidney for infection as there is a good chance for the patient to have renal function for an indefinite time. The real advantage of the Coffey operation is that it prevents obstruction of the ureter as it is implanted in a cellular space where it does not become obstructed by contraction from scar tissue. Doctor Furniss believed that in time complications can be avoided and this operation can be extended to other conditions where it will do a great deal for the comfort of the patient.

#### BONE TRANSPLANT FOR TWO-AND-A-HALF-INCH SEPARATION OF SYMPHYSIS PUBIS

DR. FREDERIC W. BANCROFT presented a woman, aged thirty-five, who was admitted to the New York Hospital, September 18, 1920, on account of a

## BONE TRANSPLANTATION OF SYMPHYSIS PUBIS

fracture of pelvis complicated by hæmatoma of thigh, with the history of having been run over by an automobile. Because the patient was so stout and because of the very large hæmatoma on the mesial surface of the right thigh it was impossible to attempt any treatment for the wide separation of the symphysis pubis.

October 5 a stab incision below the saphenous opening gave exit to approximately 20 ounces of apparently colorless clear serum. When the wound was enlarged a very large hæmatoma was evacuated. Carrel tubes were inserted. She was discharged November 18 with her wound in the right thigh healed. She was readmitted the following October. She had a waddling gait and complained of difficulty and pain on walking due to marked separation of the symphysis pubis.

November 1, 1921, a bone graft transplantation was done, as follows:—

Pfannenstiel incision over pubis. 1—Scar tissue dissected away. Both ends of the symphysis were isolated. They were separated about  $2\frac{1}{2}$  inches. There was considerable atrophy and both ends were surrounded by bursæ. Scar tissue between the fragments was separated free. Fragments were thoroughly isolated and they were beveled off on the anterior surface, leaving a free bleeding surface of cancellous bone. 2—Semi-elliptical incision over left tibia. A piece of bone including its periosteum 1 by  $3\frac{1}{4}$  inches was removed from the anterior surface. This extended down to the medullary canal which in this particular tibia was about 0.5 centimetre from the anterior surface. The muscles were sutured then over the tibia and the skin and subcutaneous tissue closed with silkworm and silk.

Gloves and instruments used in this procedure were then discarded. Piece removed was split longitudinally so that it consisted of two pieces, was then fixed to the symphysis bridging the defect, and held in place by chromic sutures, inserted through drill holes in the transplant and symphysis. Fat and connective tissue were united around the transplant as well as possible and the wound closed with silkworm gut and silk. The pelvis was immobilized as far as possible by a moleskin plaster and plaster-of-Paris girdle extending from about a little above the umbilicus to below the femoral trochanter.

*Post-operative Course.*—Pelvic wound healed *per primam*. Two years later she developed a complete prolapse of the uterus, which was repaired by performing a vaginal hysterectomy associated with repair of cystocele and perineum.

X-rays taken five years after operation showed the bone graft still in place. While very obese, she has been able to walk since operation without the waddle gait.

This case is presented because it is unusual to have a bone graft inserted in connective tissue to bridge a defect as wide as this. Apparently at the end of five years the graft still persists in its original contour.

DR. JOHN J. MOORHEAD said he had seen two cases of separation of the symphysis pubis in both of which an attempt was made to bring them together, in one case with a bone graft which was a complete failure and in the other with wire. The latter was only partially successful. This case of Doctor Bancroft's is the first instance Doctor Moorhead had ever seen of correction of this disability by any such means of stabilization. In practically all such cases there is an associated separation of the iliosacral joint, or other evidences of fracture of the pelvis.

DOCTOR BANCROFT, in closing the discussion, said that he had apologies to offer in this case. Ideally, the patient should not have needed a bone graft, for, if compression by either bandage or sling could have been applied immediately following the trauma, the separation might have been reduced. When this patient was admitted, however, she had a huge hæmatoma, containing several ounces of blood in the right thigh, she was in extreme shock, and was very obese, and it was impossible to attempt any immediate reduction. At time of operation no attempt was made to diminish the separation of  $2\frac{1}{2}$  inches of the symphysis, as it was felt that this would mitigate in the success of the bone graft. The graft was merely used to bridge the defect and to stabilize the pelvis.

#### NINETEEN YEARS' IMMUNITY FROM RECURRENCE AFTER OPERATION FOR BREAST CARCINOMA

DR. WILLIAM DARRACH presented a woman who came to Roosevelt Hospital June 29, 1911, with a history that two weeks previously she had noticed a small, hard lump in her left breast with no associated pain or tenderness. She was an enormously obese Syrian woman, forty-two years of age, pale in color with mucous membranes quite anæmic. Except for the obesity nothing abnormal was made out on physical examination, except that in the outer and left lower quadrant of the left mammary gland, a mass about 4 by 6 by 4 centimetres could be felt. It was freely movable, attached neither to the skin nor the deeper parts. The overlying skin seemed normal in character. No axillary involvement could be made out. June 30 a local incision of the mass and adjacent tissue was made, and the immediate pathological examination showed carcinoma. A complete removal of the breast and pectoral muscles, except for the clavicular head of the pectoralis major, was then carried out.

*The Pathological Examination.*—Section from nodule in breast shows cords of large polyhedral cells extending in various directions through fairly dense connective tissue. The cells in places tend to assume an alveolar arrangement, and in a few places there are still small lumina, though for the most part the cells are packed closely together. The cells have large nuclei, and there are occasional mitotic figures. The connective tissue contains scattered collections of small round cells. *Diagnosis.*—Adenocarcinoma.

She was discharged on the fifteenth day. She was seen four months later. At that time she complained of some tingling in the region of the wound and along the inner side of the arm. She could then get her hand to the top of her head and back of neck, but internal rotation was slightly limited. She reports that she gained 25 pounds since operation. About six months later she noticed an elongated, firm mass along the free margin of the right pectoral muscle. This was considered to be simply a dense mass of fat and in later examinations showed no further change. She was last examined two weeks ago and no evidence of any metastases was found. An X-ray examination of the chest at this time was negative for carcinoma.

DR. ALLEN O. WHIPPLE asked whether the microscopic report of the specimen showed carcinoma in the lymph nodes and, second, whether the patient had pre-operative and post-operative radiation therapy. Doctor Whipple said he would like to be able to report a nineteen-year interval result after operation for carcinoma of the breast; there are so many failures that

## IMMUNITY FROM RECURRENCE OF BREAST CARCINOMA

such a result was indeed encouraging. He believed that the Presbyterian Hospital could show only one similar case.

DOCTOR DARRACH replied that the pathological report showed unmistakable adenocarcinoma. In replying to Doctor Whipple's question, he said that there had been no pre-operative or post-operative radiation.

DR. ALEXIS V. MOSCHCOWITZ referred to a report presented a few years ago by his associates, Doctor Colp and Doctor Klingenstein, who looked up the statistics of Mount Sinai Hospital for a certain period. Of these cases, eighty-nine patients were followed for five years or more, and while among these cases many five-year cures were found, the number of cures became progressively less with advancing years. Doctor Moschcowitz wished to emphasize the fact that the so-called "five-year cure" is really of very little value and he has therefore substituted for this term, the less incriminating phrase "free from recurrence."

The outstanding feature of these late cases was that not one of them had a local recurrence, but all died of metastases, which leads Doctor Moschcowitz to believe that in the absence of a local recurrence, there must have existed at the time of operation, minute metastases.

Referring to the important question of pre-operative and post-operative radiation, Doctor Moschcowitz follows the advice of most surgeons and recommends post-operative radiation to all of these patients. He is willing to confess, however, that he has yet to see a positive recurrence of metastases cured by X-ray or radiation.

DR. HENRY H. M. LYLE referred to a case with a local recurrence occurring two years after a radical amputation for carcinoma of the breast in which he had assisted the late Dr. Charles Peck. This patient is alive and free from recurrence and the original operation was performed twenty-nine years ago.

DR. WILLIAM CRAWFORD WHITE said that when Doctor Darrach announced that he was going to report this case from Roosevelt Hospital, he looked up all the records of women who had been operated on prior to January, 1926, who were forty years of age or under. There were forty-seven such cases which had been followed up and twenty are still alive and free from evidence of recurrence after five years. Twenty out of the forty-seven are therefore five-year cures. Of these forty-seven, twenty-eight had axillary metastases and nineteen were free from axillary involvements. Of the twenty-eight who had axillary involvement only five were alive and free from recurrence after five years. Of the nineteen with no metastasis, fifteen were free at the end of five years. Doctor White considered it especially important that these should be regarded as primary surgical cases. There is a school of thought developing that women of forty years of age and under have such a poor prospect that it is inadvisable to give them surgery and one should resort only to radium irradiation and Röntgen therapy. It seemed to the speaker very important to depend on surgery in these cases, and to use irradiation as aids only. Doctor White thought the

protagonists of irradiation would have to work hard to show cases similar to the one presented.

DR. FRANK E. ADAIR said that this case which is reported as a nineteen-year cure suggested to his mind another case of breast cancer of long duration which offered an interesting opportunity for speculation. The case referred to was that of a patient who had adenocarcinoma of the breast. A radical mastectomy was performed. The patient remained free of any obvious recurrence during the remainder of her life—her death twenty-five years later being due to a cardiorenal condition. An autopsy was performed and much to everyone's surprise a small adenocarcinoma about 1 centimetre in diameter was found in the prepyloric portion of the stomach. The patient had given no previous symptoms of stomach cancer. Was this a metastatic nodule from the adenocarcinoma of the breast? Was it a primary adenocarcinoma of the prepylorus? In Doctor Adair's opinion fifteen years should be estimated as the reasonable length of time that any case of breast cancer should be observed, before considering the patient cured.

Referring to the results of breast cancer in women of thirty-five years or younger as contrasted with the results in women of fifty years or older, Doctor Adair stated that the reason why the disease is more devastating in the younger women is that there is a larger percentage of small cell, anaplastic, Grades III and IV types in the younger women, than in the older. In the latter there occurs a greater percentage of scirrhus type, in which case the cells are larger, well enmeshed in the fibrous network, have less opportunity for invasion of lymphatics and blood-vessels, and consequently remain localized many times for years before metastasis occurs.

#### COMPOUND FRACTURE OF HUMERUS. DIVISION OF RADIAL NERVE

DR. WILLIAM DARRACH presented a girl, four years of age, who came to the hospital February 8, 1930, with a history that five months previously she had sustained a compound fracture of the right humerus together with other injuries in an automobile accident. The lower end of the upper fragment had protruded through the skin and the wound had been infected. There was considerable drainage from the wound which persisted for about seven weeks. The wound then healed and remained closed until time of admission. At this time there was a distinct angulation forward of the humerus. X-ray examination at this time showed union of an old comminuted fracture at the junction of the upper and middle thirds with considerable overriding and angulation. Examination showed complete loss of power and sensation in the distribution of the radial (musculospiral).

February 14 an attempt was made to locate and suture the ends of the nerve. Through a vertical incision over the dorso-lateral aspect of the arm, the nerve was located, after some difficulty, embedded in a mass of dense fibrous tissue. The proximal end was found to terminate blindly in a shallow depression of the bone just proximal to the upper end of the lower fragment, the terminal 5-7 millimetres being embedded in bone tissue. The distal end of the nerve was located about 4 centimetres below this point lying in the intermuscular plane. After freeing the nerve and freshening the ends they could be approximated but under distinct tension. At this time it seemed probable that the anastomosis would not hold because of the ten-

## PARTIAL AND SUBTOTAL GASTRIC EXCLUSION

sion, but because of the child's condition, it was thought wiser to stop the procedure and the wound was closed. The child made a good recovery from the operation and the wound healed promptly.

Two months later a second attempt was made to repair the nerve. The old scar was excised and the nerve identified after considerable difficulty. It was decided to excise the old site of fracture in order to overcome the deformity but especially to allow better approximation of the nerve ends and  $2\frac{1}{2}$  centimetres of bone were removed. The ends of the bone were then approximated and held in place by a small 4-screw Sherman plate. It was found that the nerve ends had pulled apart and the ends were again freshened and then approximated with fine silk sutures. Examination of the portion of the bone removed showed distinct evidences of infection persisting in several areas. The child made a good immediate recovery, but on the third day her temperature rose to  $104^{\circ}$  and remained there for twenty-four hours. At this time the wound was opened and several ounces of thick, creamy pus allowed to escape. Following this her temperature reached normal after twenty-four hours and remained so from that time to the time of her discharge four weeks later. The sinus persisted and September 25 the plate and screws were removed through the old incision. The overhanging edges of bone were removed and the wound packed with vaseline gauze with the arm bandaged to the side. The dressing was left intact for nineteen days. Following this the outer dressing only was changed, until sixty-six days after operation when the vaseline gauze was removed. On removal, the wound was found to be covered with red, healthy granulations and comparatively little discharge. One week later the cavity had entirely filled, flush with the surface.

Five months after the nerve suture, there was distinct power in the extensor group so that the patient could extend her wrist, although the finger motions were distinctly limited. This steadily improved until at present, extension of the wrist is firm and strong and the fingers can be straightened out entirely. The abductors of the thumb are still quite limited in their power.

This case illustrates some of the late complications of compound fractures with nerve injury. There has been an unusually rapid and lucky return of function, following late nerve suture in the presence of an infected wound. It illustrates the presence of infective organisms at the site of a compound fracture even though active inflammatory signs have been absent for some time. Furthermore it illustrates the advantage of providing free drainage in infected bone followed by vaseline gauze packing which is left in place for a long period without change.

## PARTIAL AND SUBTOTAL GASTRIC EXCLUSION

DR. WILLIAM F. CUNNINGHAM read a paper with the above title for which see page 1167.

DR. HERMAN FISCHER said that this operation is not entirely new but it is undoubtedly of help in many cases where resection cannot be done, but here again, as so often in these not absolutely radical operations, one can never be sure that the patient is cured. Moreover, it is not a simple operation and its great disadvantage is that the diseased part of the stomach is left in the body of the patient. Doctor Fischer had seen massive hæmorrhage and perforation follow this procedure. However, for large ulcer at the pylorus which involves the structure of the lesser omentum, it might

be recommended. He had performed it in two cases, one patient forty-eight years of age and the other fifty-six, both of whom stood the operation well.

DR. C. J. MACGUIRE thought that this operation had a very useful rôle in occasional complicated cases; and where one is to adopt this procedure, Doctor Cunningham has shown that there is no reason to worry about the fate of the excluded segment. The evidence of rapid degeneration and atrophy is very comforting. He thought that the occurrence of jejunal ulcer would be very frequent following this procedure, unless the anastomosis to the stomach was made proximal to the pars media. In Doctor Cunningham's case the post-operative gastric analysis showed no free hydrochloric acid, so apparently the anastomosis was made sufficiently proximal to the acid-forming segment.

DR. FREDERIC W. BANCROFT showed some lantern slides of an operative technic of a modification of the Devine operation suggested by Lewis Gregory Cole and modified by himself.

This operation removes the mucous membrane from the antrum of the stomach and therefore puts the duodenal ulcer at rest in an alkaline medium.

He has had nine cases in which this operation has been performed. There have been no deaths, and only one complication—which was a jejunostomy on the sixth day post-operative, due to partial paralysis of the distal jejunum.

The details of this operation will be described in a future publication.

DR. THOMAS H. RUSSELL said that he thought that the disadvantages of this operation were: First, that the disease was not removed and that it is believed by many that a certain per cent. of ulcers of the stomach ultimately became malignant; second, on account of the dangers of perforation of the ulcer as he had had this to happen in one case following this operation; third, the dangers of gastrojejunal ulcers forming as result of not enough of the stomach having been removed.

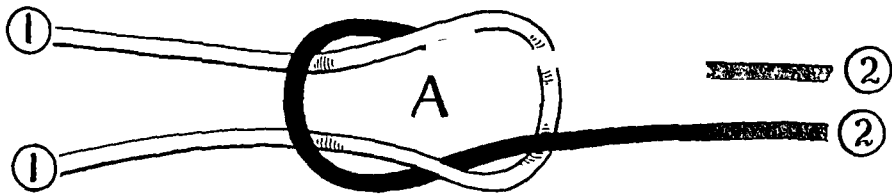
DR. LEWISOHN agreed with Doctor Russell that every gastric ulcer is potentially malignant. For this reason subtotal gastrectomy is preferable to a side-tracking operation, which leaves the ulcer in place. The method described by Doctor Cunningham was not a small procedure. Undoubtedly subtotal gastrectomy could have been performed in this case without any greater risk for the patient. The late results in subtotal gastrectomy for gastric ulcers are perfect, while a resection for duodenal ulcer may be followed in rare instances by a gastrojejunal ulcer. A resection in gastric ulcer always removes at least two-thirds of the stomach. The secondary achlorhydria following the removal of the major part of the stomach is a safeguard.

DR. CUNNINGHAM, in closing the discussion, said that he agreed with Doctor MacGuire that the area to be excluded or resected should be extensive enough to get rid of the acid-bearing portion of the stomach. There was only one point he had to add to the discussion and that was with reference to the fact that considerable trouble may be encountered in the operating room in loosening the stomach from the pancreas. This procedure shortens the time of operation and the excluded area may be resected at a later date.

# BRIEF COMMUNICATIONS

## A SECURITY LIGATURE

THERE is often a great deal of difficulty in securely tying certain inaccessible structures in surgery, such as in ligating of a cystic duct and artery after cholecystectomy. In order to assure ease in application, security in placing and tying such surgical points as above indicated, the knot to be described is proposed.



Having selected the ligature material of choice, two strands of proper length are taken and tied, as shown in the diagram, leaving a square knot "A" and two ends, marked "1" "1" and "2" "2". The part "A" fits over the clamp and the ends "1" "1" and "2" "2" are so grasped that the thumbs of the right and left hands impinge on the sides of the knot and press in the ends "1" "1" and "2" "2" respectively. This allows placing the knot as deep down over the stump to be tied as desired. By pulling in the opposite directions the two ends, "2" "2" and "1" "1", the knot "A" is securely tied and does not slip. To further assure nonslipping, ends "2" "2" or "1" "1" can be held by clamp or assistant, while the other end is being tied. Either end can now be easily tied without fear of slipping, as the end being tied is firmly held in place by the opposite ligature. The square knot is further tied at ends "1" "1", and once this is accomplished, ends "2" "2" can be readily tied with ease and without fear of anything slipping.

Thus, this gives a double ligature tie which is easily applied, which can be securely tied, and which leaves, as a final result, three square knots, one in the centre, and one on each side. If so desired, after tying ligatures "1" "1" and "2" "2", ends "1" "1" can be tied to ends "2" "2", thus leaving five square knots, one in the centre, and one in each quadrant.

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FIG. 1.—Showing relationship between the cyst and the kidney and ureter.

FIG. 2.—Showing relationship between the cyst and the caput coli. The appendix in the region of the cecum is elongated and tortuous.

SYNCHRONOUS DERMOID CYST OF THE GREAT OMENTUM  
AND OF THE OVARY

DERMOID cysts may occur in any region of the body, but are most commonly found in the ovary. The object at the present communication is to report a case in which a dermoid cyst was present in the great omentum and was associated with a dermoid of the left ovary.

CASE REPORT.—R. K., a woman, aged forty-eight was first seen November 3, 1930. She was then complaining of pain in the right side of the abdomen of three weeks' duration. The pain was dull, aching, intermittent in character, and became accentuated about one-half hour after the ingestion of food. A previous history of similar pain was not elicited. The pain did not radiate to the back or shoulder. There was no heartburn, fullness or belching after eating, and no history of jaundice. The appetite was always good and she never vomited, but had been constipated as far back as she could remember. Melæna was not present. Save for diurnal frequency, voiding every hour or two, there were no other urinary symptoms. She had lost ten pounds in weight during the previous three months. There was no cough nor night sweats.

Her past history was essentially negative save for metrorrhagia which had been present for the last year or two, evidently incidental to the climacteric. She did not appear ill. The heart action was good and the lungs were clear. The breasts were normal. The systolic blood-pressure was 162 and the diastolic 92. The abdomen was obese and lax. In the right umbilical region one could feel a freely movable, round mass of uniform hardness and about the size and consistency of an orange. It was not tender, did not move with respiration and was not fixed to the overlying abdominal wall. The rest of the abdominal examination was negative. Due to the depth of the vaginal vault, the adnexa could not be palpated.

Cystoscopy revealed a slightly trabeculated bladder with normal ureteral orifices. Both kidneys were easily catheterized. Microscopic examination of the urine from both kidneys was negative. The 'phthalein concentration from both kidneys was fair.

A right pyelogram (Fig. 1) was normal. The right kidney appeared to be of normal size, shape and position. Situated about one and one-fourth inches below the lower pole of the right kidney, and overlapping the right ilium there was a circular shadow about four inches in diameter with a well-defined border and mottling within its confines. It seemed to have no connection with the right kidney or ureter. A barium meal (Fig. 2) showed the tumor to be outside the gastro-intestinal tract.

On the sixth of November, under spinal anæsthesia, the abdomen was opened through a three-inch right mid-rectus muscle-splitting incision. The great omentum was found to be densely adherent to the anterior parietal peritoneum. Incorporated in the posterior leaf of the great omentum and adherent to the lateral abdominal parietes and to some loops of intestine, there was a hard, cystic tumor about the size of a grapefruit with a dense wall of yellowish-pink color. A cystic tumor about the size and shape of a large hydronephrotic kidney in the left ovary was also revealed. The appendix was very much elongated and densely adherent to the mesentery and the lateral pelvic wall. By careful dissection, it was possible to completely enucleate the tumor from the omentum. The portion of the omentum which harbored the tumor was resected and the appendix removed. A left salpingo-oöphorectomy was then done. Convalescence was smooth and uneventful, the patient being discharged from the hospital on the eleventh day after operation. She has been seen on several occasions since then and on February 4, 1931, her condition was excellent. She had fully recovered and had resumed her domestic duties.

The omental cyst (Figs. 3 and 5) measured  $8\frac{1}{2}$  by  $7\frac{1}{2}$  by  $5\frac{1}{2}$  centimetres. The external surface was covered with thick, parchment-like tissue which contained hæmorrhagic areas and fibrinous strands. A cut section disclosed a hollow cavity which was



FIG. 3.—Surface view of the omental dermoid cyst.

FIG. 4.—Sagittal view of omental dermoid cyst.

SYNCHRONOUS DERMoids OF OMENTUM AND OVARY

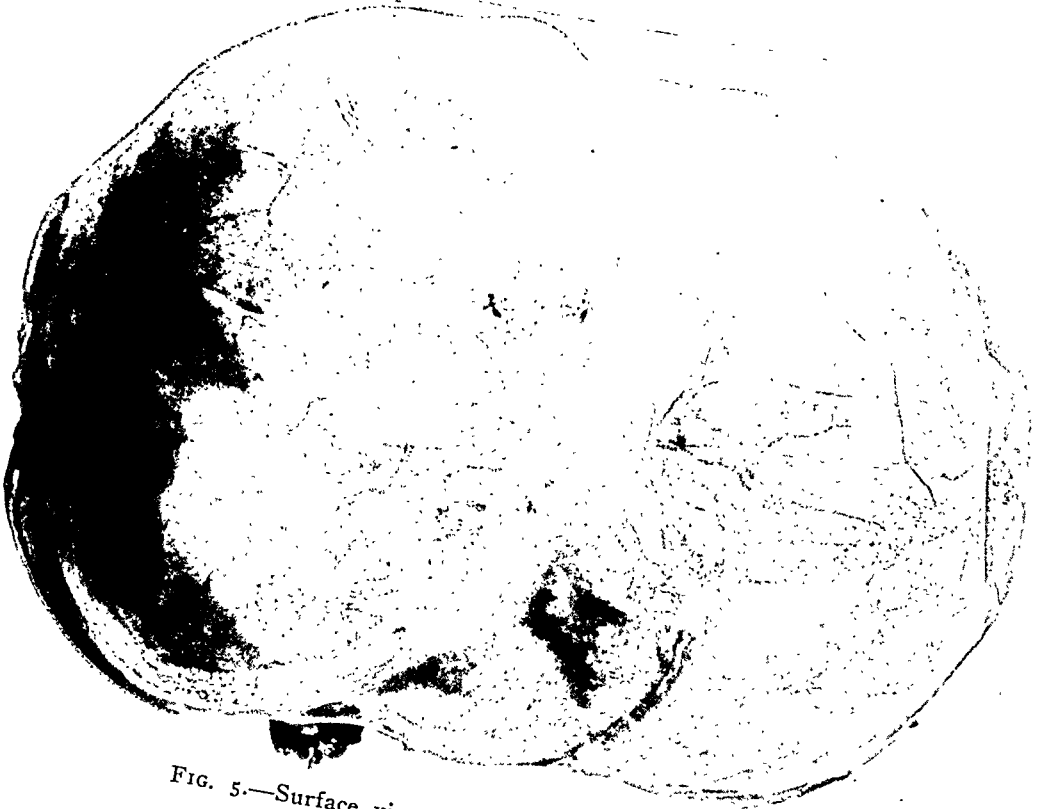


FIG. 5.—Surface view of ovarian dermoid cyst.



FIG. 6.—Sagittal view of ovarian dermoid cyst.

filled with yellowish, cheesy material in which many hairs were imbedded. The walls were firm and contained areas of calcareous deposits.

The second specimen consisted of an ovarian cyst (Figs. 5 and 6) with the attached fimbriated portion of the fallopian tube and measured 14 by 9 by 6 centimetres. The external surface consisted of parchment-like tissue which was covered with small blood-vessels and several yellowish-colored nodules measuring about 1 centimetre in diameter. The tube was firm and hæmorrhagic and in the tubo-ovarian ligament was a small mucinous cyst one-half inch in diameter. On cut section the tumor was found to be divided into four loculi. The interior was filled with a pasty, lemon-colored material in which a few hairs were imbedded. The cyst-walls were smooth. At one pole of the tumor there was a small cyst one-half centimetre in diameter.

Histologically, both the omental and ovarian cysts were typical dermoid tumors containing inspissated sebum and numerous areas of calcareous deposits.

In a review of the literature, Mumey found only fourteen cases of dermoid cysts of the great omentum reported up to 1928. Abbe, in 1895, reported a case of a dermoid cyst involving the great omentum which was associated with a dermoid of the left ovary which also contained a mucous cyst, simulating the case here reported. As far as our review of the literature goes, the total number of dermoids of the great omentum, including the one here reported, is sixteen.

The first case to be reported was by Lebert, in 1734, and the next by Laflize, in 1792 (Quoted by Mumey.) Meckel reported another in 1815. Since then isolated cases have been added to the literature.

These tumors seem to predominate in the female in the ratio of 8 to 1. It has been suggested by observers such as Sajous that they are detachments from the ovaries which become imbedded in the omentum during menstruation or pregnancy. Lexer and Bevan are of the opinion that they are formed in the pre-natal period by the incorporation of a fragment of ectoderm in the great omentum during the closure of the abdominal wall. Some have advanced the theory of trauma and heredity as etiologic factors, but it is hard to conceive how these factors can play a causative rôle in the production of these tumors.

Dermoid cysts of the omentum produce no pathognomonic symptoms. The patient usually complains of a vague pain or heaviness in the abdomen and may feel a swelling over the involved area. Should the tumor impinge upon a loop of intestine, pressure symptoms may result, giving rise to vomiting, constipation and melæna. Asthænia and loss of weight may occur. A tumor lying low in the abdominal cavity may be detected by vaginal or rectal examination. Röntgenograms are useful adjuncts in the establishment of a diagnosis, particularly when the tumor cyst is calcified and contains opaque material such as teeth and hair. These tumors must be differentiated from mesenteric cysts, ovarian cysts, lienal, hepatic and renal tumors, lipomata and aortic aneurysm. The presence of a round, movable, firm tumor near the anterior abdominal wall, especially in a female, warrants further investigation to rule out this type of tumor.

The prognosis depends upon the early recognition of the tumor and im-

## PERFORATING ULCER OF COLON

mediate removal before any complication arises, such as intestinal obstruction or infection. Perforation of the cyst with resultant peritonitis, although possible, is exceedingly rare. Recurrences following extirpation have not been reported.

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## PERFORATING SIMPLE ULCER OF COLON

THE rarity with which simple ulcers of the colon eventuate in perforation may warrant the publication of two more cases which have recently come under my observation.

CASE I.—A man, fifty-nine years of age, came under my care at the Union Memorial Hospital February 1, 1930, with a history of chronic indigestion and in the recent past of having attacks thought to be biliary colic. He stated that he had taken a saline purgative every day for many years. The present illness had started two days before admission but his symptoms became decidedly worse a few hours before coming to the hospital. When admitted, he was suffering with severe pain in the right upper quadrant, the right lower quadrant and right lumbar region. He had had a bowel movement the day before admission. His temperature was 102.4° and white blood count 17,200. He was a stout man; the right half of the abdomen was very rigid and tender with some tenderness in the right flank. An acute abdominal condition was recognized but the exact diagnosis could not be stated. A few hours after admission, a right rectus incision was made which revealed a peritonitis of the entire right side of the abdomen rather well limited to this side of omentum. A violent inflammatory reaction with œdema and induration of all structures in this neighborhood in a very fat abdomen made it difficult to determine the exact situation but the escape of gas led to a perforation of the intestine. It was thought best to do an enterostomy. This was done by suturing a catheter in the perforation with a purse-string suture and draining the abdomen freely with cigarette drains, endeavoring to leave unbroken the protecting omental wall. The next day the patient seemed improved but did not drain through the catheter and had a silent distended abdomen. The second day enemata and irrigation of the tube were ineffectual. Gastric lavage showed dark foul stomach contents. A duodenal tube which was left in, drained the same kind of material. All efforts to relieve the obstruction were unavailing and he died February 3, 1930. Autopsy showed a perforated simple ulcer about the size of a lead pencil at the hepatic flexure with several small ulcers in the neighborhood, each containing an enterolith but only one being perforated. There was general distention of the intestine with a diffuse right-sided peritonitis. The gall-bladder and appendix were normal. There were no ulcerations of the stomach, duodenum or other portions of the intestinal tract.

CASE II.—The following patient was operated upon by Dr. Frank Lynn, from whom the data have been obtained with permission to report the case.

A male, aged thirty-three years, was admitted to the University Hospital August 5, 1929, suffering from severe abdominal pain located in the left lower quadrant. In May, 1929, he was in the hospital on account of a similar attack. A diagnosis of diverticulitis

of the sigmoid was then made. His symptoms subsided so that he was discharged as improved. He now returns with a recurrence of his former symptoms. August 5, 1929, a mid-line laparotomy was done. On opening the peritoneal cavity, a quantity of murky fluid escaped. The appendix was sought and while it was found to be large, it showed no evidence of an intense inflammation. In the left iliac fossa was considerable exudate surrounding the sigmoid. Inspection revealed a perforated ulcer, 1 centimetre in diameter, covered over with exudate. This was closed over with mattress sutures of fine silk. The appendix was then removed. A small gridiron stab wound was made in the left side and a rubber tube inserted for drainage and the mid-line incision closed. For the first few days following operation, the patient was rather uncomfortable because of accumulations of gas, but after an enæma on the fifth day after operation he was very much relieved. The tenth day after operation he developed a right-sided phlebitis which necessitated his remaining in bed longer than at first anticipated, but on the date of discharge, August 31, the incision had healed completely, the swelling in the right leg and thigh had disappeared and he was free of any pain.

Barron, in a memoir in the Archives of Surgery of September, 1928, reviews fifty previously reported cases of simple ulcer of the colon and adds three. Boyer and Tuft, in the Journal of the American Medical Association, May 17, 1930, report a simple ulcer of the ascending colon with infiltration mistaken for malignancy, for which a radical resection was done. They quote a case reported by W. Moll: *Zentralbl. f. chir.*, vol. liii, p. 2274, September 4, 1926, which does not seem to be included in Barron's group of fifty-three. The other cases spoken of by Boyer and Tuft are included in Barron's review.

Moll's case was one of simple ulcer of the cæcum which had not quite perforated but was apparently in danger of perforating at any time. Examination showed no signs of malignancy.

In Surgery, Gynecology and Obstetrics, May, 1930, Barron reports another simple ulcer of the cæcum which perforated and recovered after closure and drainage. The cases outlined herewith make the fifty-seventh and fifty-eighth cases to be reported. Close scrutiny of some of the cases described makes one doubtful whether all should be classed as simple ulcers.

Among the fifty-eight cases thus collected, there were forty-five perforations. These were located as follows: Cæcum, 17; perforations, 11; Ascending colon, 14; perforations, 12; hepatic flexure, 4; perforations 4; transverse colon, 0; perforations, 0; splenic flexure, 5; perforations, 4; descending colon, 2; perforations, 1; sigmoid colon, 12; perforations, 11; rectum, 4; perforations, 2.

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### DIAPHRAGMATIC HERNIA IN AN INFANT\*

Two years ago we reported a case of a three-and-one-half-months-old infant who had an incarcerated diaphragmatic hernia, who was operated upon and who made a complete recovery,† and who now at the age of nearly three is apparently normal in every

\*From the Surgical and Pediatric Service of the Michael Reese Hospital.

†The Journal of the American Medical Association, vol. xcii, pp. 2014-2016, June 15, 1929.

## DIAPHRAGMATIC HERNIA IN AN INFANT

respect. Since then we have seen several cases in children of hernia of the diaphragm at the œsophageal opening in which, because of the mildness of the symptoms, no operation was advised. Recently, however, we have had the opportunity to observe a case which was the counterpart of the one previously described.

The child was brought to us by Doctor Kohn, her uncle, who has observed her and treated her since birth and to whom we are indebted for an excellent history of her condition up to the time of operation. The child was born nine months previous to admission normal in every respect. She took her feedings well from the breast and later from the bottle. When she was about six months old she had her first "colic" and since then has had "colics" frequently. With the "colics" there was often respiratory embarrassment but for the most part the symptoms were chiefly gastro-intestinal in nature, vomiting, apparent pain, etc. One very interesting feature which was noticed was that at no time during these



FIG. 1.—Röntgen plate before operation after a small barium meal. Note the stomach in the abdominal cavity but a great portion of the intestinal tract in the left thorax.



FIG. 2.—Röntgenogram taken seven days after operation. Note the complete expansion of the left lung and the replacement of the heart and mediastinum to its normal position. Note the normal contour of the diaphragm.

so-called "colics" was the abdomen distended, but on the other hand the abdomen remained soft, and, if anything, seemed smaller than before. The significance of this was not appreciated until an X-ray examination was made and the diagnosis of diaphragmatic hernia established. From the time the child was six months old until she was brought to us for operation the "colics" seemed to be increasing in severity and frequency. The mother had noticed for several months that the respiratory movement of the left chest was less than the right, also that the infant's respirations were comparatively rapid. At the time of admission to the hospital the baby weighed seventeen pounds, looked and acted like a healthy, happy, well-nourished baby of nine months of age. On physical examination no other congenital abnormalities such as club feet, cleft palate, supernumary fingers, *etc.*, were observed. The chest appeared normal in size and contour. The respiratory motions on the left side were relatively decreased and on the right side markedly increased. Per-



cussion and auscultation of the right chest revealed no abnormalities other than that the heart and mediastinum were shifted well to the right. The left side of the chest was flat on percussion and no breath sounds could be heard. Examination of the abdomen was negative for abnormalities. The X-ray examination was interesting. After a barium meal the stomach seemed to fill normally and so did the duodenum and apparently the upper jejunum; after this the barium appeared above the diaphragm until practically the entire left chest was opaque. A barium enema showed that both the splenic and the hepatic flexures were fixed below the diaphragm in their normal relative positions but that the cæcum was in the chest cavity. The opening in the diaphragm seemed to be lateral—a condition later verified at operation. The heart and mediastinum were shifted to the right. The left lung was apparently collapsed. When the child was held in the upright position there seemed to be no tendency of the hernia to reduce itself.

In view of our excellent result in the case previously reported, in view of the fact that this infant was older and better nourished and especially in view of the fact that the "colics" in our present case were increasing in severity and frequency, we unhesitatingly advised operation. We waited until the child should have overcome whatever ill effects

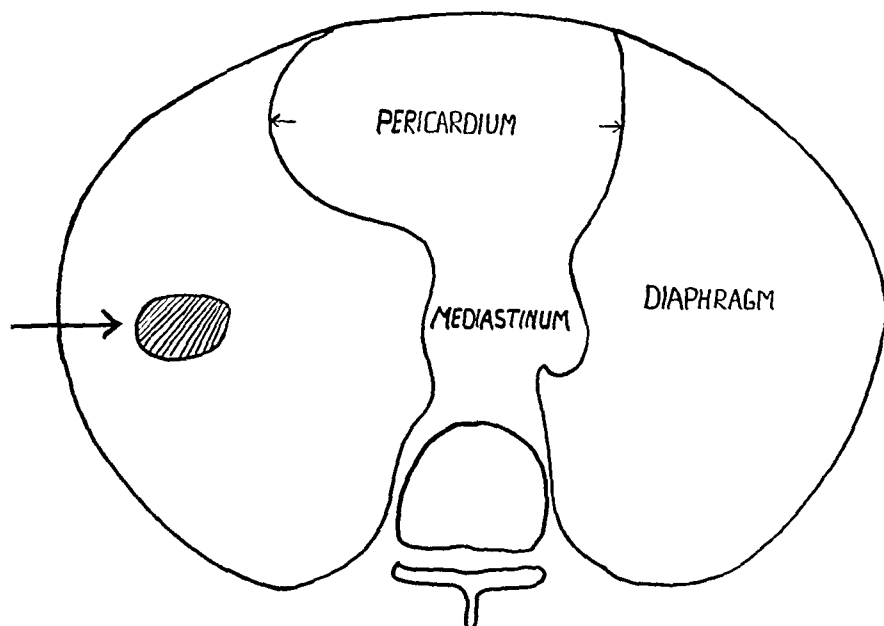


FIG. 3.—Diagram showing position of the hernial opening in the diaphragm.

there might have been from the small barium meal and enema, and for a few days longer until we were sure that the child was well conditioned to the hospital.

The operation was performed under an ethylene, oxygen, ether-pressure anaesthesia—as are all our intrapleural operations.

We do not use any special apparatus other than the usual (in this case infant-sized) gas mask. The pressure is regulated by varying the force of the gas flow into the mask and the outflow through the outlet valve. We are fortunate in having an excellent anaesthetist who has had a large experience in giving anaesthetics for operations in which the pleural cavities have been opened, and we have found that we have been able to dispense with intratracheal catheters, special respiratory or differential pressure machines, *etc.*

The child was placed upon the table lying on the right (healthy) side and the table tilted so that the head was higher than the feet. This was to facilitate the reduction of the hernia and the retention of the intestines in the abdominal cavity once they had been reduced. The incision started just posterior to the posterior axillary line and followed

the ninth interspace to the costal margin and then swept upwards towards the left border of the sternum. Great care was taken to clean the parietal pleura in the ninth interspace so that the pleural cavity could be opened under direct inspection lest the underlying bowel be injured. After the pleural cavity was opened a ligature was passed about the ninth rib, and another posterior to it. The rib was cut between. The ligatures were then firmly tied so as to control bleeding and the incision into the pleura extended into the eighth interspace. The tenth rib was similarly dealt with. Rib spreaders were inserted and the pleural cavity inspected. The entire left pleura was filled with loops of intestine. The cæcum with its attached appendix occupied the extreme apex. Apparently the entire ileum and a large portion of the jejunum were in the chest instead of in the abdomen. A muscle-splitting incision was now made in the left hypochondrium and two fingers of the operator's right hand introduced into the abdominal cavity up to the hernial opening. By gentle traction on the mesentery from below and gentle pressure on the loops of bowel from above, the hernia was gradually reduced. The reduced bowels were of necessity allowed to prolapse through the abdominal incision and wrapped in towels saturated with warm normal saline solution. After the entire intestinal contents of the chest had been reduced it was found that the opening in the diaphragm was about three-fourths inches in diameter, situated in about the mid-axillary line and midway between the pericardium and the chest-wall (see diagram [Fig. 3]), that is, apparently not at the site of any natural embryologic opening. It was found that the diaphragm was sufficiently relaxed so that the opening could be closed by imbrication, bringing the anterior edge fully one-half inch over the posterior lip. Before this was done the peritoneal surface of the anterior lip and the pleural surface of the posterior lip—the lining above and below was apparently the same—were scarified with a scalpel so as to stimulate adhesions. The imbrication was held with interrupted silk sutures. After all the sutures were tied the site was carefully palpated from below to preclude the possibility of bowel having been caught in the suture. Inspection through the chest wound showed that there was a fair degree of tension on the diaphragm at the suture line and so the eleventh rib was broken subpleurally and pushed slightly inwards, thus reducing the size of the diaphragmatic arc. The left lung at the beginning of the operation was entirely atelectatic and held firmly against the hilum; under the influence of the pressure of the anæsthetic it gradually expanded. At first it had been my idea to expand it completely before closing the pleura but on further consideration we decided that it might be safer to expand it only partially, close the chest-wall firmly and then allow further expansion to take place gradually as the pneumothorax which remained became absorbed. The chest wound was tightly closed by passing catgut sutures around the ribs above and below the pleural incision and firmly suturing the overlying muscles and fascia. The intestines were replaced in the abdominal cavity and the muscle-splitting wound firmly sutured. In many ways the replacing of the intestines which had been allowed to prolapse through the abdominal wound because the abdomen appeared almost too small to accommodate them constituted the most difficult part of the operation, and the tension on the abdominal wall after this was done proved how fortunate we were in having made a muscle-splitting incision rather than the much easier left rectus incision.

The child left the operating table in fair condition, but with an extremely fast pulse and respiratory rate. An oxygen tent with the oxygen at a pressure of about 50 per cent. was found useful in diminishing the respiratory effort. Otherwise the post-operative care consisted of the usual post-operative regime plus hypodermoclysis of normal saline and glucose solution. The chief trouble post-operatively came from a partial paralytic ileus of the intestines. However, after repeated small enemata, the insertion of an anal dumbbell and repeated passing of a stomach tube, normal peristalsis occurred and from then on the convalescence was uneventful. The oxygen tent was removed on the fourth day at which time the respiratory rate was 44. Immediately after removal of the tent the rate increased to 52, but within twelve hours was back to 44. At no time did there appear to be any pleuritic effusion. The left lung expanded promptly and by the seventh day, judging from a röntgenogram taken at that time, was already completely expanded. By that time,

## BRIEF COMMUNICATIONS

furthermore, the heart and mediastinum had assumed a normal position. The child was taken home on the fourteenth post-operative day apparently perfectly well.

### SUMMARY

A nine months' old infant with a left sided congenital diaphragmatic hernia which became incarcerated, was operated upon, the hernia reduced and the diaphragm repaired. The child recovered from the operation and now two months later is apparently cured.

An abdominal as well as an intercostal incision were required to reduce the hernia. The abdominal incision was a muscle splitting one so as to withstand the increase of intra-abdominal tension after the reduction of the intestine into the peritoneal cavity.

The ribs which formed part of the arc of the diaphragm were fractured in order to reduce the arc and thus allow an imbrication of the diaphragm.

The imbricated portions were scarified to promote the formation of adhesions.

The chest was closed without drainage.

The atelectatic lung expanded completely in less than seven days.

In this case, as in the case of the infant reported two years ago, although all the physicians who had seen the case realized that without operation the child would surely die from intestinal obstruction, most of them advised against operation.

We feel that the time has long since passed when intra-thoracic operations should be looked upon with such dread as to be decried especially in the face of an otherwise incurable condition.

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## STAB WOUND OF HEART

THIS case is reported for two purposes. 1. To demonstrate the impossibility of raising the arterial blood pressure when the heart is compressed by a large amount of blood in the pericardium.

2. To emphasize the value of the method of Beck\* of placing a stay suture in the apex of the heart when closing a defect in the heart muscle.

CASE REPORT.—Patient S. S., a husky negro male, age twenty-two, was stabbed in the left chest with scissors. Immediately he walked two blocks and collapsed in a physician's office. He was given morphine and sent by automobile twenty miles to the Vanderbilt Hospital. On entrance to the hospital, he was cold and sweating and his pulse was weak. The arterial blood pressure was 75/40 millimetres mercury. He complained of thirst and of abdominal pain. A small puncture wound about 0.5 centimetre long was seen in the sixth interspace on the left about six centimetres from the mid-sternal line. X-ray examination revealed a heart shadow which was thought to be slightly larger than normal. There was no pneumothorax or hemothorax.

He was given 1000 cubic centimetres of normal salt solution intravenously. This

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\* Beck, Arch. Surgery, vol. xiii, p. 205, 1926.

## STAB WOUND OF HEART

caused no alteration in his blood pressure. A little later, he was given 400 cubic centimetres of blood by direct transfusion. The blood pressure remained the same and the pulse continued to be barely perceptible. Immediately after the transfusion, a median sternotomy was performed and the pericardium was exposed. The pericardium was so tense that it was difficult to grasp it with forceps. When it was opened, blood spurted upwards to a height of about eighteen inches. Immediately after the incision into the pericardium, the anæsthetist stated that there was an improvement in the volume of the pulse. A stay suture was placed in the apex of heart as described by Beck\* in his work on experimental animals, and the position of the heart could be altered at will by making traction on the thread. The wound was located in the left ventricle near the apex just lateral to the descending branch of the left coronary artery. It was about  $1\frac{1}{2}$  centimetres in length and there was very little bleeding from it at the time. It was closed with interrupted sutures. The incision in the pericardium was partially closed and the two halves of the sternum were approximated by the use of encircling sutures of silver wire. At the completion of the operation the blood pressure was 115/80 millimetres mercury.

The post-operative course was essentially uneventful except for the drainage for several days of clear fluid through the centre of the incision. At the present time, six months since his injury, he appears to be entirely well.

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## BOOK REVIEW

JOHN CHALMERS DA COSTA. SELECTIONS FROM PAPERS AND SPEECHES. Cloth; octavo; 440 pp. Philadelphia, W. B. Saunders Co., 1931.

The literature of medicine would miss much if it were deprived of the personal reminiscences with which some of its practitioners have, from time to time, enriched it. The textbook contributions which succeeding decades have brought to the tables of medical men may be considered as the daily food of the profession. But when to these are added biographical sketches and essays into fields of general literature, more interesting and captivating contributions present themselves. It is no longer the daily bread that is being offered to us, but the *hors d'œuvres* and the desserts, perhaps even the beverages and the cigars that are being added to the menu. Such contributions give a special grace and attraction to professional life and when, as repeatedly happens, a physician makes valuable contributions both to the daily bread of his profession and to the lighter and more pleasing elements of its life, he occupies a position worthy of the highest praise. It is in this latter category that the author of the book before us is to be placed.

Among his fellow townsmen who have preceded him along this path, we find Gibson and Gross, Mitchell and Osler, Agnew and Keen—surely an attractive company in which to find oneself. The papers which make up this book reflect, in a pleasing way, the special gift for wit and wise criticism possessed by its writer, with which for all these many years he has illuminated the lecture room in which his teaching has been carried on. The themes which have occupied the attention of Doctor Da Costa in this series of addresses, are most varied, from "The Trials and Triumphs of the Surgeon" to "The Personal Side of Pepys," and from "Medical Paris during the Reign of Louis Philippe," to "Suicide." We can commend to the special notice of the surgeon the list of aphorisms, fifty-four in number, with which he concludes his address on "The Trials and Triumphs of the Surgeon."

It is difficult, perhaps unnecessary, to make comparisons as to the relative merits of these various addresses. The reviewer, however, has found himself most intensely interested and instructed by the sketch of Baron Larrey. There is, however, not an uninteresting page in the whole book.

L. S. PILCHER.

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